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CLINICAL ASPECTS OF INTESTINAL OBSTRUCTION

D. J. CURRIE, M.D., M.Sc., F.R.C.S. (Edin.), F.R.C.S.(C), D.S.*

THE intestine is said to be obstructed when there is an interruption to the onward flow of the intestinal contents. The obstruction may be in the lumen (fecal impaction, polyp, foreign body, intussusception, gall stone, mass of worms), in the bowel wall (stricture, atresia, paralytic ileus, tumor, regional ileitis) or outside the bowel (adhesion, hernia, band, tumor, inflammatory mass, volvulus). The cause may be obvious clinically (fecal impaction, tumor mass or an irreducible hernia) but generally it is not, although it may at times be very difficult, from the practical point of view it is important to try to determine the type of obstruction that is present so that the proper treatment can be given. The obstruction may be due to simply a paralysis of the intestinal musculature and the relief of this obstruction with conservative treatment alone may be expected. It may be due to a mechanical blockage of the bowel in which case one can take a little time to prepare the patient for an early, rather than an emergency operation. However, the blood supply to a part of the bowel may be blocked and the intestine in imminent danger of necrosis and perforation. In this case, urgent operation is required. Intestinal obstructions will be discussed according to these three broad groups and the important exceptions to this classification in so far as treatment is concerned will be noted.

I. PARALYTIC ILEUS

The intestinal muscle becomes paralyzed and intestinal tonus disappears. Peristaltic waves do not occur and the bowel dilates. Thus the cardinal signs are absolute constipation (obstipation), abdominal distension and regurgitant vomiting without any crampy abdominal pain.

Paralytic ileus is always a secondary disorder and may be caused by trauma or disease of intra- or extra-abdominal organs or by biochemical disturbance. Paralytic ileus follows, at least in some degree, every abdominal operation. It commonly accompanies biliary, appendiceal or renal colic and torsion of ovarian cysts. Post-operative acute gastric dilatation is a form of paralytic ileus. (Post-operative urinary retention due to atony of the bladder musculature is a related condition). Paralytic ileus commonly accompanies inflammation of abdominal organs (cholecystitis, appendicitis, pancreatitis, salpingitis) and is always present when the peritoneum is irritated (peritonitis, perforated viscus, intraperitoneal hemorrhage). The most common cause of paralytic ileus is peritonitis. Paralytic ileus accounts for the meteorism of pneumonia, coronary occlusion, renal infections, uremia and fracture of spine, ribs or pelvis. Paralytic ileus may be caused by biochemical disturbances as in potassium deficiency, chronic morphine poisoning or anoxia due to mesenteric vascular occlusion.

As paralytic ileus is always a secondary condition, the clinical picture will vary according to the primary disorder. However, the features of paralytic ileus itself are worthy of description. The patient first suffers the steady discomfort of abdominal distension and there is complete constipation of both feces and gas. Anorexia, nausea and often hiccoughs are shortly followed by the regurgitation of mouthfuls of brownish fluid. The drowsy patient may not realize

*St. Michael's Hospital, Toronto.

when this regurgitant vomiting occurs and aspiration of this material into the trachea is a dreaded complication. The vomiting is not marked until late except in cases of acute gastric dilatation. There is no crampy abdominal pain because the intestinal muscle is paralyzed.

The patient lies quietly on his back in no obvious distress. The abdomen is distended and no peristaltic waves are seen. The abdomen seldom moves on respiration because of the distension. The abdomen feels ballooned and tense and is hyperresonant on percussion. Only if the primary condition causes peritoneal irritation will there be hyperesthesia, rigidity and rebound tenderness. On auscultation there is dead silence. Frequently the transmitted breath or heart sounds are heard with cavern-like clarity. Clinical evidence of dehydration is late because vomiting is generally late.

In the absence of a primary inflammatory lesion the pulse and temperature are normal. The blood pressure and hemoglobin are normal unless there has been an internal hemorrhage or strangulation. The leucocyte count is raised in inflammatory lesions, intra-abdominal hemorrhage, intestinal perforation or strangulation. An x-ray of the abdomen with the patient supine shows gas-filled loops of small bowel with some gas in the colon and often a large gastric gas shadow. An x-ray with the patient erect shows multiple gas-fluid levels in the small and large bowel with a large gastric gas-fluid level. Free gas in the peritoneal cavity due to perforation of the stomach or duodenum may be seen underneath the diaphragm when the patient is x-rayed in the erect position. When the dilated loops are confined to one region, that region should be carefully examined for a primary inflammatory lesion (the right lower quadrant loops of appendicitis, the central sentinel loop of pancreatitis, the pelvic loops of pelvic peritonitis). By x-ray, the walls of the dilated loops of bowel appear thickened in peritonitis.

The signs of peristaltic activity indicate the recovery of obstruction due to paralytic ileus. The patient begins to feel a few crampy abdominal pains and passes some gas by rectum. The discomfort of distension improves and the abdomen becomes smaller and feels softer. The normal bowel sounds reappear.

The treatment of paralytic ileus is conservative. The stomach is kept empty by a gastric tube and continuous suction. Intravenous fluids are prescribed to correct water and electrolyte imbalances. Heat may be applied to the abdomen but peristaltic stimulants are not given. One may confidently await recovery on this conservative regimen provided that the primary condition causing the paralytic ileus requires no further treatment. It is most important to recognize the cause of the paralytic ileus. When the primary condition is not obvious one must proceed with caution and examine the patient frequently. Three conditions (perforated viscus, internal hemorrhage and mesenteric vascular occlusion) cause paralytic ileus but deserve special mention because they are serious conditions which are not always easily recognized and require immediate operative treatment.

Paralytic ileus after trauma to the abdomen suggests perforation or intraperitoneal hemorrhage. The sudden onset of severe steady abdominal pain with signs of peritoneal irritation and paralytic ileus suggests a perforated peptic ulcer. On the other hand, the sudden cessation of severe crampy abdominal pain with beginning peritonitis and paralytic ileus suggests a perforated appendix, gallbladder or cecum. There is free gas in the peritoneal cavity when a peptic ulcer or the cecum perforates but not when the gallbladder or appendix ruptures. Generally the severe board-like

rigidity, the early reflex vomiting and obstipation without marked distension are present and help to distinguish these lesions.

Intraperitoneal hemorrhage causes both paralytic ileus and peritoneal irritation. The patient may be in distress because of severe steady abdominal pain. The patient is pale, restless, and thirsty. Respirations are increased in rate and depth. Again the signs are those of paralytic ileus with peritoneal irritation but in addition there is usually shifting dullness. Intraperitoneal blood remains fluid (because of dilution) except near the bleeding organ. Thus the clotted blood may produce a boggy pelvic mass (ruptured ectopic pregnancy) or a left upper quadrant non-shifting area of dullness (ruptured spleen). The hemorrhagic type of shock with low blood pressure and weak pulse with falling hemoglobin along with a history of a blow to the left lower chest or left upper quadrant of the abdomen or the first missed period of a pregnancy, suggests the correct diagnosis. The leucocyte count generally rises when there is free blood in the peritoneal cavity.

The sudden onset of severe steady abdominal pain accompanied by marked neurogenic shock and paralytic ileus suggests an intra-abdominal strangulation. Torsion of an ovarian cyst is the common cause but must remember that the intestine may become strangulated in the absence of mechanical obstruction of the bowel. Such is the case in mesenteric vascular occlusion which is usually due to an arterial embolus or a venous thrombosis. The source of the embolus may be found (auricular fibrillation, mitral stenosis, endocarditis, atheroma, aneurysm) and often the patient passes a fluid stool with gross blood because infarcts of the bowel are almost always of the hemorrhagic type. Mechanical intestinal obstruction with strangulation will be considered separately.

II. MECHANICAL OBSTRUCTION

The four classical features of intestinal obstruction are present—colicky pain, complete constipation, abdominal distension and vomiting. Unlike paralytic ileus, simple mechanical obstruction is a primary condition. When all age groups are considered together, the more common causes are, in order of frequency, bands and adhesions, external herniae, neoplasms, volvuli, and intussusceptions. When the lumen becomes blocked, peristaltic contractions increase in force in an attempt to force the intestinal contents past the obstruction. The bowel proximal to the occlusion becomes distended with accumulated fluid and gas; the distal bowel soon empties itself.

The pain is primarily crampy (colicky) in nature and is felt in the peri-umbilical region in small bowel obstruction and in the hypogastrium in colonic obstruction. Gurgling abdominal noises (borborygmi) are heard along with each cramp. These noises may localize the obstruction. The colic is severe and tends to increase in severity and frequency. After a time the bowel becomes fatigued and the crampy pain is replaced by the steady discomfort of distension. Constipation is complete as neither feces nor flatus are passed by rectum except for that which is contained in the bowel distal to the obstruction. Only one or at the most two bowel movements may follow the onset of a high intestinal obstruction. Consequently complete constipation may not be obvious in the recent onset of acute mechanical obstruction. Vomiting begins early and is reflex rather than regurgitant in nature. The higher the site of the obstruction, the earlier the onset of vomiting and the clinical signs of dehydration, and the later the appearance of distension. The lower the obstruction, the later the vomiting and dehydration but the abdomen becomes distended earlier. The distension becomes more marked the

longer the obstruction has been present. Finally in large bowel obstruction there may be no vomiting but only anorexia or nausea, no dehydration but gross abdominal distension. Conversely, in pylorie stenosis, vomiting is very early, dehydration and electrolyte imbalance are marked, and there is no gross distension. Pain is not a feature of pyloric obstruction. These observations are of great importance in determining the level of the obstruction. At first the vomitus is yellowish acid gastric juice. Clear greenish (bile-stained) alkaline vomitus indicates regurgitation of duodenal contents into the stomach. Later, thick, malodorous, black (bloody) or orange colored stagnant small bowel contents indicate a well established, fairly low complete bowel obstruction.

On examination the patient is moderately distressed because of the severe crampy pains and the vomiting. Between pains the patient is fairly well composed and is not pale or perspiring as if in shock. Abdominal distension is marked in lower obstructions but may not be obvious in high intestinal obstructions. In early obstruction the distension tends to be central in small bowel obstruction and in the flanks in colonic obstruction but later the distension is general in both. In a patient with a thin abdominal wall and marked small bowel distension the dilated loops may be seen lying transversely across the abdomen. In low incomplete small bowel obstruction peristaltic waves may be seen running transversely back and forth across the abdomen. In high duodenal or pyloric obstruction the gastric peristaltic waves pass from left to right. Clinically peristaltic waves are not seen in the colon. If peristaltie waves are seen in colonie obstructions it usually means that the ileo-cecal valve is incompetent and these peristaltie waves are due to small bowel contractions. If the ileocecal valve becomes incompetent it usually means the bowel obstruction has been present for some time. These peristaltic waves are most marked in cases of low colonic obstruction which for a time has been incomplete (carcinoma of colon). Borborygmi may be heard and these will correspond with the visible peristaltic contractions and the crampy pain suffered by the patient. The hernial orifices must always be examined. Obstructed irreducible inguinal, femoral or ventral herniae are the second most common cause of mechanical bowel obstruction.

On palpation one may feel the intestinal movements due to exaggerated peristaltic contractions and one may find an area of tenderness over the site of the obstruction. One must carefully palpate all hernial orifices for a mass or for tenderness. One should also palpate for tumor masses. The sausage-shaped mass due to an intussusception may be found in the epigastrium. Curiously a large tense ballooned volvulus of the cecum may be found in the left lower quadrant. A volvulus of the sigmoid colon may be felt in the right lower quadrant. On auscultation, the gurgling sounds of gas and fluid being churned by excessive peristaltic contractions are obvious and generally the exaggerated bowel sounds are maximal over the site of the obstruction.

The pulse, blood pressure and temperature are normal. If the obstruction is high, vomiting and dehydration will be marked and this will cause dryness of the tongue and lips, soft sunken eyeballs, weakness, prostration, oliguria and a dry breath (there will be little fogging of a glass held in front of the open mouth). Dehydration causes hemoconcentration and is shown by high hemoglobin and hematocrit determinations. The leucocyte count is often elevated.

Normally very little gas is seen by x-ray of the abdomen except for the gastric gas bubble. In bowel obstruction gas-

filled loops of bowel are seen proximal to the occlusion. Dilated jejunum may be recognized by its central position and by the fine serrations and indentations (valvulae conniventes) in its outline. The distended ileum is central and has a smooth, even outline. The colon shows the bulgings of the haustrations and it lies peripherally. The cecum distends like a smooth balloon. An x-ray with the patient erect shows gas-fluid levels corresponding to the dilated loops. Central fluid levels, like the dilated loops of small bowel on the supine x-ray, fold back one upon another in transversely running rows (ladder-rung pattern). The highest gas-fluid level on the left side is the gastric bubble. Peripheral levels are usually in the colon.

As the obstruction continues the bowel immediately proximal to the obstruction becomes fatigued and the bowel dilates passively owing to fluid and gas. More proximally the colicky contractions continue and further fill the fatigued bowel and the abdomen distends. In colonic obstruction the ileo-cecal valve at first functions so that although the colon fills, the small bowel remains relatively empty. The cecum is the weakest part and bears the brunt of the distension. It can dilate to enormous dimensions but it is the first part to perforate and this is a real hazard in colonic obstructions. Colonic obstructions are almost always closed-loop obstructions.

The treatment of simple mechanical obstruction is at first conservative. Continuous gastric suction and intravenous fluid therapy are prescribed. Arrangements are made more or less at leisure for early operative treatment. Under these preparatory measures, occasionally a volvulus will untwist or a hernia will reduce. Patients who suffer recurrent intestinal obstruction due to adhesions and who have had multiple operations for this may be treated by small bowel decompression using a long suction tube because often these obstructions will be relieved by these conservative measures. Generally an operation is necessary. Under anesthesia the abdomen is palpated for a mass. Although this may not make the diagnosis, it will at least allow the surgeon to make his incision in the proper region. On opening the peritoneal cavity, there is usually some serous or perhaps some blood-tinted fluid. The site of the obstruction is found and the simplest operation which will relieve the obstruction is performed. If one suspects strangulation (signs of shock and peritoneal irritation) or colonic obstruction (which is a closed-loop obstruction) or a closed-loop small bowel obstruction (as an external irreducible hernia), operation becomes more urgent and should be carried out without delay.

III. INTESTINAL STRANGULATION

Intestinal strangulation may be a primary condition (mesenteric vascular occlusion or abdominal injury with torn mesentery) with obstruction due to secondary paralytic ileus. However, strangulation generally follows an acute mechanical bowel obstruction when the constricting lesion affects not only the intestinal lumen but also the vessels supplying the bowel wall. Thus a patient often gives a history of having a hernia or a previous operation and the present illness begins as a simple mechanical intestinal obstruction.

In addition to the four classical features of mechanical obstruction (colicky pain, obstipation, distension, vomiting) there are signs of peritoneal irritation and the patient is in shock. The crampy pain of strangulation is usually as frequent and as severe as in the most severe case of mechanical obstruction. In addition there is steady abdominal pain because of peritoneal irritation and this pain may help to localize the site of the strangulation. Because of the steady pain, the patient is never entirely free

of pain and this steady pain continues just as intensely after gastric suction is established as before in contrast to the crampy pain. Mesenteric vascular occlusion and spasm along with anoxia of the bowel wall also causes severe adbominal pain. There is complete constipation with the exception that loose bloody movements may be passed in cases of intussusception, mesenteric vascular occlusion and volvulus. Vomiting is usually early and severe. There is general weakness, prostration and fear of impending disaster. Thirst varies according to the amount of vomiting and internal bleeding.

On examination the patient is in serious distress and appears shocked with pallor, cold perspiration and rapid breathing. Abdominal distension varies with the level and duration of the obstruction. Distension is seldom pronounced unless strangulation is preceded by long standing mechanical obstruction. Peristaltic waves, if seen, soon disappear and paralytic ileus begins. The hernial orifices require very careful examination as even a very small hernia may be the site of strangulation. Tenderness in a hernial orifice is a most important sign. The strangulated bowel causes peritoneal irritation so that there is hyperesthesia, muscular rigidity and rebound tenderness. As in mechanical obstruction, one may be able to palpate a tender hernia, a tender intussusception, a tender volvulus or a boggy doughy mass of strangulated intestine in mesenteric vascular occlusion. Tenderness is almost invariably maximal over the strangulated bowel and rebound tenderness usually points to that region.

The pulse is usually thin, thready and rapid and the blood pressure is low because of the shock and blood loss. The temperature is subnormal in the early stages because of shock but may rise later because of peritonitis. The hemoglobin and hematocrit values usually drop because of hemodilution due to blood loss, rather than rise because of hemoconcentration due to the fluid loss in vomiting. The leucocyte count is generally elevated because of peritonitis and blood in the peritoneal cavity. The x-ray changes resemble those of mechanical obstruction. There is nothing specific about the radiological changes of strangulation. If there is time, x-rays will indicate the level of the obstruction and may show gas in the strangulated loop (volvulus or hernia). One must remember that strangulation can occur with little or no evidence either clinically or radiologically of obstruction.

Once the diagnosis of strangulation is made, an intravenous infusion is started and blood is taken for cross-matching for a blood transfusion. A gastric tube is passed and suction is used to empty the stomach completely so that a general anesthetic may be given safely. A short delay may be necessary to transfuse or to correct severe fluid and electrolyte disturbances in a very ill patient. Then if one should suffer an academic turn of mind and wish to contemplate the cause of the strangulation, only ten minutes is allowed. This ten minutes is spent in scrubbing for the operation. Under anesthesia, a mass may be felt and this will direct the surgeon to make the proper incision. On opening the peritoneal cavity there is bloody or obviously blood-tinged fluid as opposed to the clear or slightly blood-tinted fluid in simple mechanical obstruction. The simplest operation is performed which will relieve the obstruction and strangulation. Necrotic bowel must be removed from the peritoneal cavity. During or immediately after operation a blood transfusion is almost always required.

The differentiation of bowel obstructions into these three groups may seem to be of little value as often one finds that a combination of these types can be

recognized in a clinical case of bowel obstruction. A portion of the bowel always suffers paralytic ileus in a strangulated obstruction and usually the portion of the bowel proximal to a mechanical obstruction becomes fatigued and also suffers paralytic ileus. The bowel adjacent to an inflammatory lesion suffers from paralytic ileus whereas the proximal bowel lying farther away develops excessive peristaltic contractions resembling a mechanical obstruction with crampy abdominal pain. Nevertheless, if the case is studied to determine the order of appearance of the various forms of obstruction, a correct diagnosis can generally be made. The wise surgeon is always alert to diagnose certain combinations which indicate conditions requiring urgent treatment—mechanical obstruction of the colon or of a closed-loop of small bowel, mechanical obstruction with peritoneal irritation and shock (obstruction with strangulation), paralytic ileus with hemorrhagic shock and often peritoneal irritation (intraperitoneal hemorrhage) and paralytic ileus with neurogenic shock and often peritoneal irritation (ruptured viscus and mesenteric vascular occlusion).

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PYREXIA OF UNKNOWN ORIGIN

W. J. McILROY, 5T6

FEVER of unknown origin is a diagnostic problem which is faced frequently by every practising physician, and a systematic approach to the problem is necessary for all of us. The term is difficult to define, and the question arises of how extensive an investigation should be conducted before a case may be diagnosed as such, if it may be considered a diagnosis at all. Oppel and Berntsen have gotten around the problem of definition by considering as cases of pyrexia of unknown origin (PUO) all patients referred into hospital by practising physicians where the diagnosis could not be established outside of hospital.

Since fever is a manifestation of such a wide variety of conditions, it becomes necessary in considering the individual case to exclude many possible diagnoses in favour of the more probable ones. The results of the study made by Oppel and Berntsen cast considerable light on this aspect. They studied a series of 110 consecutive cases admitted to the New York Hospital in 1951–52 with the diagnosis of PUO. 23% of their cases recovered in a short time without a specific diagnosis being made. 27% suffered from a respiratory tract infection and this was most frequently upper. The remaining 50% of their cases presented a wide variety of disease states, most commonly being infectious mononucleosis, genito-urinary tract infections, gastroenteritis, subacute bacterial endocarditis, and hepatitis. They pointed out that about 8–10% were long term PUO's with conditions such as tuberculosis, tumors, lymphomas, and collagen diseases appearing in this group.

In deciding upon the more probable diagnoses, attention should also be given to the age of the patient. Although a great many diseases have no age boundaries, others show a definite age incidence. Hence, in considering the older patient conditions such as carcinoma, arthritis, collagen disease become more important, whereas in the

younger patient tuberculosis, infectious mononucleosis, rheumatic fever are common entities.

CLASSIFICATION*

A. FEBRILE ILLNESSES OF SHORT DURATION

B. PROLONGED FEBRILE ILLNESSES

I. INFECTIOUS DISEASES

1. Tuberculosis
2. Bacterial Endocarditis
3. Brucellosis
4. Salmonella Infection
5. Pyogenic Infection
6. Amebiasis
7. Histoplasmosis
8. Coccidioidomycosis
9. Schistosomiasis

II. COLLAGEN DISEASE

1. Disseminated Lupus Erythematosus
2. Periarteritis Nodosa
3. Rheumatoid Arthritis
4. Rheumatic Fever
5. Erythema Nodosum
6. Allergic Purpura

III. NEOPLASTIC DISEASES

1. Carcinoma and Sarcomas
2. Hodgkin's Disease

IV. HEMATOPOIETIC DISEASES

1. Leukemias
2. Hemolytic Episodes

V. VASCULAR DISEASES

1. Temporal or Cranial Arteritis
2. Thromboembolic Disease

VI. MISCELLANEOUS

1. Liver Disease
2. Sarcoidosis
3. Drug Fever

VII. MALINGERING

C. RELAPSING AND RECURRENT FEVERS

1. Malaria
2. Relapsing Fever
3. Rat-bite Fever
4. Pyogenic Infection
5. Hodgkin's Disease
6. Periodic Disease

*Based on Harrison—"Principles of Internal Medicine."

A. FEBRILE ILLNESSES OF SHORT DURATION

Little space will be devoted to this category since, although these illnesses are common in practice, they rarely present any difficulty to the physician. They are most commonly infectious in origin, and those in which the specific diagnosis is obscure are probably viral in origin. The bacterial infections are often readily diagnosed by culture, and treated by antibiotics. It is not often practical to try to isolate and identify the viruses, and so these illnesses are treated symptomatically.

B. PROLONGED FEBRILE ILLNESSES

A glance at the above classification is sufficient to make one realize the complexity and difficulty of diagnosis of a fever falling into this group. It is here that an orderly, systematic approach is imperative in order to arrive at a diagnosis. A combination of history, physical examination and carefully selected laboratory tests will all be needed.

I. INFECTIOUS DISEASES

The advent of antibiotics in recent years has greatly changed the picture in this category, but there are still certain infections which do not respond to the more routinely administered antibiotics, and so these conditions must be kept in mind in diagnosis.

1. *Tuberculosis:* The onset of symptoms in tuberculosis is frequently insidious, and the development of fever may often be the first symptom to appear. The fever usually begins as a slight elevation of temperature in the late afternoon or evening. This may recur daily, gradually reaching higher levels or subside and reappear intermittently. Fever is also character-

istic of an acute onset of tuberculosis, and may rise quickly to levels of 104–105°F.

Diagnostic facilities for tuberculosis are improving with the advent of routine miniature chest X-rays on admission to hospital and through the mass surveys conducted throughout the community and industry. The tuberculin test is also of assistance in diagnosis. A negative skin reaction will rule out tuberculosis in almost every instance, and a positive reaction, although it only indicates a sensitivity to tuberculin, may suggest the need for further investigation with respect to tuberculosis.

2. *Bacterial Endocarditis:* This diagnosis should be suspected in every patient with an unexplained fever, and a heart murmur. Streptococcus viridans is still the chief offender, and is highly sensitive to penicillin, but antibiotic resistant organisms may also occur. Every effort should be made to culture the infecting organism so that the sensitivity to antibiotics can be determined, but in the case of repeated negative cultures and the clinical picture of bacterial endocarditis, treatment with large doses of penicillin should be started on the basis of clinical judgment without waiting too long for positive cultures.

3. *Brucellosis:* With the pasteurization of milk, Brucellosis is rare in the city dweller. However, the disease should be considered in persons, who, through their occupation might come in contact with infected animals. Hence, the disease occurs most frequently in farmers, livestock producers, slaughter house workers, and veterinarians. Diagnosis may be confirmed by means of the agglutination reaction and blood culture.

4. *Salmonella Infection:* The incidence of salmonella infection is closely related to the degree of sanitation in an area. Typhoid can usually be traced to a carrier or an infected water supply. Diagnosis of typhoid is usually not difficult since cultures of blood or feces may be positive, and specific antibodies are detected by means of the agglutination reaction. Other salmonella organisms are more difficult to isolate, but most laboratories are equipped to carry out the necessary agglutination reactions. Salmonella infection should be suspected in any case of unexplained fever in which leukopenia, gastro-intestinal or joint symptoms occur.

5. *Pyogenic Infection:* A symptomless, localized area of pyogenic infection, inaccessible to antibiotics may cause a prolonged fever. For example, a localized mediastinal or subdiaphragmatic abscess may be diagnosed only with the aid of X-ray studies. If considered, however, infections of this nature may frequently be demonstrated.

6. *Amebiasis:* Amebiasis is more prevalent and severe in tropical countries, but it has a world wide distribution. Amebic colitis or dysentery is more easily diagnosed than amebic liver abscess. Stool examination is only positive in 30–50% of cases, and so if the disease is suspected, a therapeutic trial of an anti-amebic drug such as chloroquine or emetine may help to establish the suspected diagnosis.

7. *Histoplasmosis:* This condition is recognized most frequently in the Midwestern United States. The disease is at first pulmonary, but later may involve any part of the body. The organisms may be found in smears from the lesions, in monocytes of the blood or by biopsy. A positive skin test with histoplasmin is usual.

8. *Coccidioidomycosis:* Coccidioidomycosis is most common in California. Infection is primarily pulmonary, but cutaneous lesions are common.

The characteristic fungus is usually easily found in the tissues. The skin test is positive.

9. *Schistosomiasis:* This condition is endemic in Africa, but is not seen in this country. Diagnosis is made by biopsy, or by demonstrating the ova in the feces or urine.

II. COLLAGEN DISEASE

This group of diseases of uncertain etiology, previously thought unrelated, is classified together since involvement of collagen and interstitial ground substance of connective tissue is common to all. Systemic diseases of collagen may present with one or more of the following clinical features: arthritis, endocarditis, pericarditis, pleuritis, and scattered vascular lesions. Since fever is a constant manifestation of diseases of this group, they must receive due consideration in the case of a prolonged febrile illness.

1. *Disseminated Lupus Erythematosus:* This is a chronic, often remittent, but usually ultimately fatal disease showing a striking predilection for young females. It is not an uncommon disorder. The presence of the characteristic butterfly rash across the bridge of the nose, and the malar eminences in a patient suffering from fever and any of the other systemic manifestations, greatly facilitates the diagnosis, but does not appear in all cases. The demonstration of LE cells in the serum is strong support for the disease.

2. *Periarteritis Nodosa:* Periarteritis nodosa is a form of panarteritis affecting the medium sized arteries and arterioles of the body. The distribution of the vascular lesions is variable, presenting a wide variety of clinical manifestations in many systems of the body. Hypertension occurs in well over half the cases, and the association of this finding with continued pyrexia of unknown origin is suggestive. There is a definite male predominance. Leukocytosis is usual, and in some cases a marked eosinophilia is noted. The only conclusive method of diagnosis is through biopsy.

3. *Rheumatoid Arthritis:* This is essentially a disease of young people and is three times as common in females as in males. Early diagnosis may be quite difficult, and may even be impossible until the more characteristic features develop. Fusiform swelling of the proximal interphalangeal joints of the fingers is almost pathognomonic. Weight loss and muscle atrophy, most prominent about severely involved joints are also characteristic. The sedimentation rate is usually elevated during the active stage of the disease.

4. *Rheumatic Fever:* Rheumatic fever is thought to be a sequela of a group A hemolytic streptococcal infection and is among the first three causes of death between the ages of 5 and 30 years. The onset of the disease may be gradual, or acute with the temperature reaching levels of 102–104°F within a few days, and accompanied by rapid pulse, profuse sweating, severe prostration and polyarthritis. The striking feature of the arthritis is its migratory character, spreading from one set of joints to another. Cardiac involvement is one of the most common features. Laboratory findings indicate a W.B.C. of 15,000–25,000 cells per cu. mm. and an elevated sedimentation rate. The sedimentation rate is a good index of the rheumatic activity. An elevated antistreptolysin "O" titre is present in 80% of cases.

5. *Erythema Nodosum:* This disease is characterized by the formation of symmetrical, nodular erythematous, painful swellings on the shins or forearms. A polyarthritis commonly precedes or follows the skin mani-

festations. It is thought to be a hypersensitivity to a variety of agents, and has been associated with beta hemolytic strpetococcal infections, coccidioidomycosis, tuberculosis, and certain drug hypersensitivity reactions.

6. *Allergic Purpura:* Allergic purpura may present a diverse symptomatology. There may be articular, pulmonary, abdominal and renal involvement as well as the constitutional symptoms of fever and malaise. Diagnosis is difficult when skin and mucous membrane involvement is not present. The capillary fragility test and platelet count are normal.

III. NEOPLASTIC DISEASE

In a patient in the cancer age group, neoplasm should always be considered as a cause of fever. Pallor from anemia, loss of weight, and other more specific signs and symptoms will aid in diagnosis, but in their absence, neoplasm must be considered until proven otherwise. In Hodgkin's disease (10–15% of cases), the fever may follow the characteristic Pel-Ebstein pattern and may suggest the diagnosis before lymph node involvement is recognized.

IV. HEMATOPOIETIC DISEASES

1. *Leukemia:* The problem in leukemia is one of treatment and not diagnosis. The characteristic changes in the blood and bone marrow and the rapidly developing anemia may establish the diagnosis. However certain cases of aleukemic leukemia are difficult to diagnose at the outset. Fever is nearly always present and in acute leukemia may be associated with chills, not to be confused with infection.

2. *Hemolytic Episodes:* The hemolytic diseases are characterized by fever but the hemolytic process in itself usually steers the physician in the correct direction in discovering the cause of the fever.

V. VASCULAR DISEASES

In addition to the vascular lesions associated with the collagen diseases, temporal arteritis, and thromboembolic disease should also be mentioned.

1. *Temporal Arteritis:* Temporal arteritis or giant-cell arteritis is a generalized systemic disease of older people with a predilection for branches of the carotid artery. It is characterized locally by pain over the temporal or occipital artery distribution, occasionally visual disturbances due to involvement of the central retinal artery, and systemically by fever, general malaise and fatigue. Unlike periarteritis nodosa, to which it has been linked, it is a self-limiting disease which can be controlled by cortisone until it remits spontaneously.

2. *Thromboembolic Disease:* Thrombophlebitis is usually easily recognized, but occasionally a slight fever in a patient confined to bed is the only indication of an underlying thrombophlebitis in the deep leg veins. The patient should be watched carefully for evidence of pulmonary emboli.

VI. MISCELLANEOUS

1. *Liver Disease:* A low-grade fever unaccompanied by leukocytosis and lasting for weeks or months has been seen in about 50% of patients with Laennec's cirrhosis.

2. *Sarcoidosis:* Fever in sarcoidosis is unusual but may occur.

3. *Drug Fever:* Drug allergy is an important cause of fever, and if suspected, the drug should be withdrawn. Drug fever occurs most commonly in the second week of treatment but may occur much earlier. Hence, in investigating any case of PUO, the patient should be questioned as to medications.

C. Relapsing and Recurrent Fevers

The diseases categorized in this section are rare in this country with the exeeption of Hodgkin's disease. Malaria, although uncommon in North America, is still a major medieal problem in other parts of the world, and during the war there was a high index of morbidity amongst our troops in India, Africa, the Middle East, China and Burma.

Investigation

In the investigation of a case of pyrexia of unknown origin, as for any other diagnostie problem, the importanee of history and physical examination eannot be stressed too strongly and any additional time spent in this phase of the examination is usually rewarding. The initial elinieal impressions then form the basis upon whieh laboratory tests are ordered. There is a tendency to rely too heavily on the laboratory for diagnosis, and one must remember to keep its use in proper perspective. The sensible way to use the laboratory is to order tests in series, rather than a whole barrage of tests at one time. When the more promising elinieal impressions have been investigated and the diagnosis is still obseure, further laboratory tests may be ordered. Laboratory tests are expensive, and too often patients are subjected to a number of unneeessary proeedures. Throughout the investigation the patient should be re-examined frequently to pick up any ehanges or new developments whieh might influenee the eourse of further investigation.

Sometimes a therapeutie trial may help to establish the suspeeted diagnosis. Henee, emetine may be used in amebie lever abseess, salieylates in rheumatie eonditions or quinine in malaria.

The Value of Laboratory Tests

Oppel and Berntsen made some interesting observations on the value of laboratory procedures in their series of cases. Most of the positive laboratory findings were made by cultures and smears. Serological reactions while frequently done were rarely of any value. (1 positive Widal and 4 positive heterophile agglutinations in a total of 346 serological tests.) Less common but helpful tests were marrow aspirations, biopsy and liver funetion tests.

It is interesting to note that the laboratory proeedures of greatest value are often those of culture and smear, whieh are actually easily performed.

Conclusion

In conelusion it should be emphasized that although the eauses of fever are many and may represent diseases affecting every system in the body, an orderly approach to the problem, investigating the more probable eauses rather than all the possible eauses, and keeping in mind the relative frequeney and ineidenee of the various conditions, should reduee the number of cases ultimately left with the diagnosis of PUO.

Acknowledgment

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APHASIA

A. S. TRIMBLE, 5T6

APHASIA is defined by Nielsen as "the loss of power to comprehend or express signs and symbols, by which man communicates with his peers, due to an organic lesion of the brain." It is, then, a symptom of acquired disease and this functional language disturbance may be utilized in the localization of the disease process. The study of aphasia is difficult and tedious, made so by attempts of various investigators through the years to emphasize either the anatomic, physiologic or psychologic factors involved as well as to compile a multitude of terms and synonyms both redundant and of little clinical use. This article will attempt to present the ontogenetic development of language, some of the common syndromes seen and a method of examination.

Ontogenetic Development

AUDITION. In the development of language, the initial procedure is the perception of sounds by the baby and the development of memory patterns of these sounds for future reference. The transverse temporal gyrus of Heschl, which is the cortical station for hearing, serves only for the perception of sound. Memory pictures (engrams) of these sounds are then developed in Wernicke's area, a crescentic area of cortex in the superior temporal convolution. Repeated stimulation fortifies certain memory pictures, while lack of it leads to deterioration of the engram patterns of others and loss of recognition of these sounds. It appears that there are different locations for the engrams of words and sounds in Wernicke's area, while music

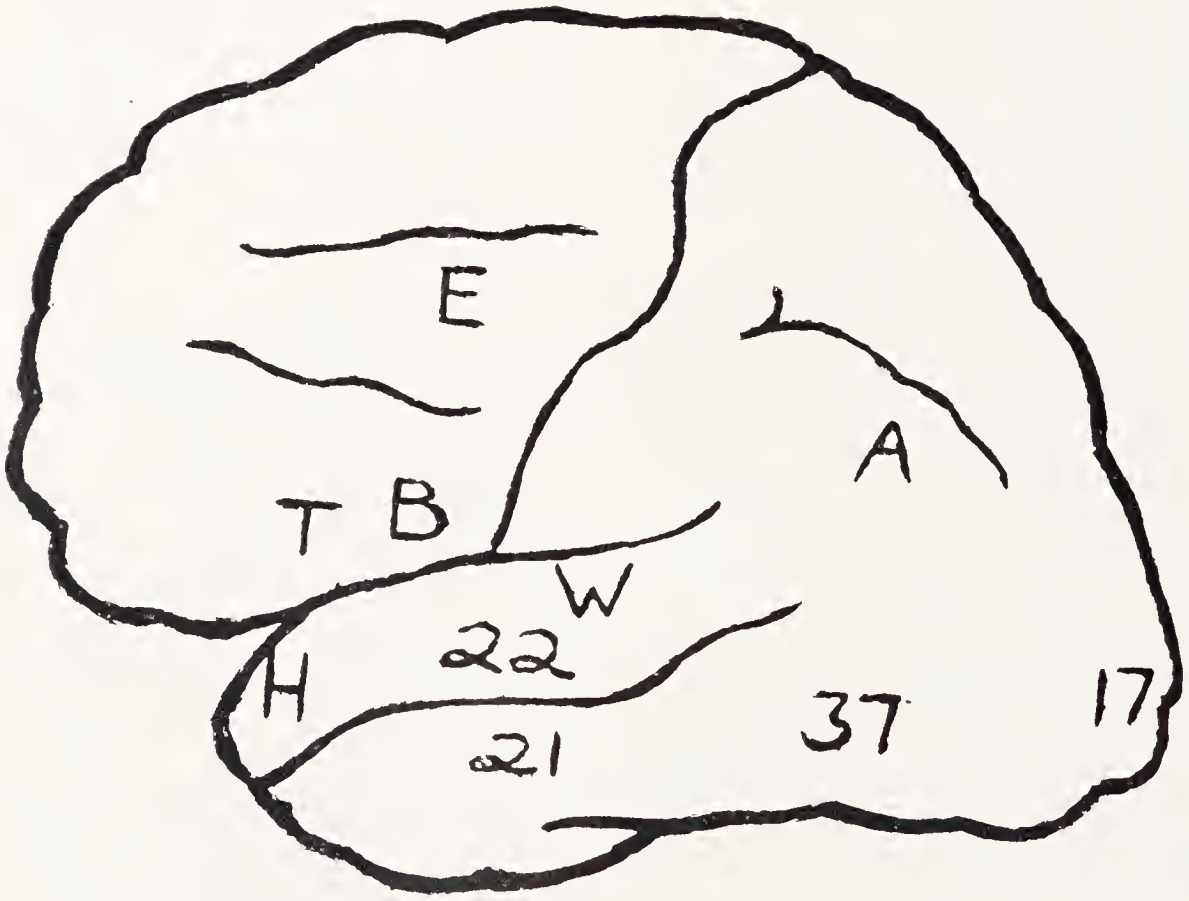

FIG. 1.—Diagram of lateral surface of cerebral hemisphere. E—Exner's Writing Centre. B—Broca's Convolution. T—pars triangularis. H—Henschen's music centre. W—Wernicke's area. A—angular gyrus. Brodmann's areas—37, 21, 22, 17.

sound engrams are retained in the tip of the temporal lobe. Also, due to the hereditary predominance of left-brained individuals the engram patterns come to be retained mainly in the major hemisphere and while the minor hemisphere retains the same potential it remains relatively undeveloped, with the result that lesions of the major hemisphere disrupt the mechanism completely and suceessful therapy depends upon the development of the dormant minor hemisphere areas. This generalization applies to almost all types of aphasia and agnosia.

The eomprehension of words or the ability to determine their significance depends on the utilization of many asoeiation areas in the greater part of the cortex, but a primary word meaning centre has been postulated to exist in area 37 of Brodmann in the temporal lobe. The development of comprehension is a high level function and follows upon perception and recognition.

VOCALIZATION. After the auditory mechanism has developed to a certain degree, the infant tries to repeat eertain sounds it has heard and in most cases these sounds are ones that through repetition have become "engraved" in Wernicke's area. The word is apparently heard silently and through an association with the speech mechanism it is vocalized. This process is earried out through stimulation of cells in Broca's area at the foot of the 3rd frontal convolution of the major side which in turn activate Betz eells in the precentral motor cortex concerned with the stimulation of the muscles of the tongue, lips, mouth and larynx necessary to produee sounds. Repeated stimulation of Broea's eortex leads to the development of engram patterns of the movements necessary to produce various sounds, but there are no speech patterns in this area.

As development proceeds, a language formulation centre is formed in area 37 of Brodmann and in the posterior parts of areas 21 and 22 by engrams of recall of words which govern the proper expression of thought as well as grammar and rhetoric. It is in this area that the proper expression of eoncepts is controlled and it is intimately associated with Broca's area, where engrams of the movements necessary are retained, by way of the external capsule.

READING. As the infant grows older visual sensation develops with the perception of objeets and symbols dependent upon the intaetness of area 17 of Brodmann lying on each side of the ealcarine fissure. Engram patterns for objects are developed in the occipital and occipital-parietal cortex on both sides of area 17 while those for written or printed words are laid down in the major angular gyrus. A separate area for mathematical figures is also said to exist. As in hearing, these engrams only account for the recognition of objects and words, while the eomprehension of words seems to be developed again in area 37 as well as in other cortieal association areas of the major hemisphere.

In association with the visual engram, auditory and motor ones are formed, so that, in reading the angular gvrus and Wernicke's area for reeognition and Broca's area for movements, are aetive. Higher centres of eortex ineluding area 37 are necessary for the determination of the significance of that whieh is read. In time, the repeated stimulation strengthens the visual, auditory and kinesthetic impressions so that eventually the movement engrams become unneeessary and only visual and auditory memories are utilized. Thus, if the patient's education is poor, he may still require movement sense to read properly and a lesion in Broca's area produces difficulty in reading.

WRITING. Children begin writing by copying letters and this initiates engram patterns in the angular gvrus separate to

those utilized in reading. It has been shown clinically that in copying a figure, such as a flower, that cannot be read, the impulses travel from the visual centre to the angular gyrus and then on to the writing centre in the frontal cortex from which impulses initiate the proper hand movements. In copying a symbol that can be read, such as a word or number, the impulses take a longer route for they are classified with the higher centres for reading before being passed on to the writing centre. The writing centre is in the second frontal convolution in the major hemisphere. It does not write automatically but is under the influence of the angular gyrus where images, letters and words are revisualized; the language formulation centre where grammar and rhetoric are formulated; and Wernicke's area which appears necessary in the revisualization process; and the interparietal sulcus where numbers are engrammed. In turn, these secondary centres react in response to the higher cortical processes where thoughts and ideas originate.

It is to be understood that the foregoing presentation has been greatly simplified and that many anatomic, physiologic and psychologic aspects have been combined into one theory that has stood the test of clinical study, but in reality is very superficial.

Classification of Aphasia

The classification of this subject can become extremely complex and while the following may be too generalized, it serves to give a basis for the understanding of the subject which could be broadened by more intensive reading.

SENSORY APHASIA. This form of aphasia involves the first part of Nielsen's definition previously given; that is, the complete or partial inability to comprehend written or spoken words. In the complete form there is no response to verbal or written command, for, although the patient can hear or see the demand, he is unable to determine its significance; however, not infrequently, he is able to imitate the action desired if the interviewer performs it.

In its incomplete form this aphasia tends to affect predominantly the names of objects and their abstract qualities. In these cases the patient may open his eyes when asked to open his mouth or pick any coloured pencil when asked to select a red one. Also in these cases, the defect is increased as the question is made longer and more complex, so that he may respond to simple demands but may fail to understand complicated orders. The comprehension of written matter is also grossly defective.

It has been previously noted that the area involved with word significance, 37 of Brodmann, is also essential to word formulation so that it is not strange to have defective word recall in this type of aphasia. In the most severe form this is called jargon aphasia and consists of unintelligible words or sounds, while in a milder degree it is seen as defective sentence structure and faulty word arrangement. "There is so much of it that and then there is so many things to do and so much to do to tell it . . ." is an example of this type.

Word amnesia is also commonly seen so that a pen is called "something to write with" but in these cases, if the examiner then offers the suggestion that it might be a pen, the patient often immediately recognizes the word as being correct. Commonly certain words are utilized repeatedly so that in the above example any number of objects may be subsequently called pens. Also there is a common tendency in this aphasia to respond to different questions with the same answer.

To a similar degree writing is involved so that unrecognizable scrawl or word omission is apparent in spontaneous

writing and on dictation. At times the ability to copy is retained.

MOTOR APHASIA. This type of aphasia corresponds to the second part of Neilsen's definition, the inability to express signs and symbols of speech. It is rarely an isolated defect, usually accompanying other speech disorders. The movements necessary to emit sounds are not involved in this type of aphasia, but their proper organization is disturbed. Because of a disruption in the engram pattern in or associated with Broca's area there is a defect in the ability to integrate the movements necessary to produce speech. There is no defect in word formulation in this type of aphasia. In the severe form no words may be uttered, but occasionally in emotional situations there is a sudden outburst of swearing, words or even sentences but such words are not true expressions of thoughts and are considered by some to be due to activity of the minor hemisphere.

In milder degrees or during recovery simpler words are correctly used or with some defect, "I can seek the thock" for "I can say the thought." Often words said correctly are continually repeated. The mildest degrees of motor aphasia are characterized by slowness, hesitation, difficulty in finding words, incorrect or mutilated words and poor speech rhythm.

Agraphia or inability to write is also present in motor aphasia.

Method of Examination

Because of easy fatiguability of the aphasic patient and gross laxibility of his speech at various times, it is essential that any examination be carried out in quiet surroundings and consist of multiple, brief interviews.

WORD UTTERANCE. The initial greeting and subsequent conversation with the patient will elicit any defect in this capacity. Defects may also be shown in his answers to questions concerning the development of his illness or his occupation—in his reply to short direct questions or in his ability to repeat words or phrases. Defects commonly seen include a limited vocabulary of simple or familiar words, repetitions, incorrect words and unintelligible sounds. Omission of syllables, and hesitation should also be noted as well as swearing and emotional outbursts.

COMPREHENSION OF SPEECH. The patient's response to requests of increasing complexity is studied to elicit defects in this sphere of the speech mechanism. Commands should test his ability to point out named objects, and perform simple and then more complex acts. An example might include "Point to your nose," then "Point to your nose with your left hand;" then "Point to your nose with the index finger of your left hand and rub your stomach with your right hand"—tests using his ability to properly distribute coins can also be done.

WORD RECALL AND FORMULATION. To differentiate the presence of agnosia (inability to recognize) the patient should be asked to name objects shown to him, such as a pen or wallet and also differentiate between colours. The higher level or aphasic level of this defect is the loss of significance of the names of these objects, thus he should be asked to point them out by name or select from a list of words those that are foods. His ability to recall days of the week, months, alphabet and numbers is also investigated.

THOUGHT EXPRESSION. This is best studied by the patient's attempts at normal conversation, his ability to extract, from a picture, the meaning and express it, or his ability to respond to simple questions in a positive or negative way. Mistakes to be noted include word omissions, faulty grammar and sentence structure and hesitations.

READING. As with comprehension of speech, commands of increasing difficulty are written out and the response is noted. The patient should also be asked to explain the meaning in complex sentences and to read such sentences aloud.

WRITING. If the patient has a letter he has written this should be studied and he should also be asked to write the names of objects and descriptions of pictures. His ability to write on dictation, translate print in script and to carry out arithmetical problems should be tested.

In these tests when the patient has a paralyzed right extremity it may be necessary to utilize blocks and printed cards instead of a poorly writing left hand.

SUMMARY

An attempt has been made to simplify the complicated subject of aphasia into a logical and clinically usable form by reviewing the ontogenesis of language, the anatomical and physiological localization, the common types of motor and sensory aphasia, and a brief method of examination.

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COXSACKIE VIRUS DISEASES*

S. M. SUMI, 5T6

THE initial strains of this group of viruses were first recovered from two patients with paralytic poliomyelitis, and they were first described by Dalldorf and Sickles in 1948.[5]

These viruses produce characteristic lesions and death in suckling mice and hamsters, but are not lethal to the older members of the same species. On the basis of the difference in lesions in susceptible animals and in the disease in man produced by these viruses, Dalldorf distinguished two groups of viruses—A and B. On the basis of immunological differences these viruses have been further differentiated into serologically distinct types. Nineteen different types of group A and five types of group B viruses have now been identified.

Laboratory diagnosis of Coxsackie virus infection is based on the isolation of the virus from the throat and stool, and the demonstration of a rising titre of antibodies in the patient's serum specific to the virus isolated.

Clinically, the group B viruses are responsible for Bornholm disease and certain cases of aseptic meningitis, and have been implicated in acute myocarditis in infants.[9] The group A viruses are thought to cause herpangina,[8] summer "grippe" and three-day fever.[16]

CLINICAL MANIFESTATIONS

A. SYNDROMES DUE TO THE COXSACKIE B VIRUSES

I. BORNHOLM DISEASE

This is an acute infectious disease also known as epidemic pleurodynia and epidemic myalgia. It was first described in Norway in 1872. Coxsackie Group B virus was first isolated

*Read before A.O.A. January 1956.

from a case of epidemic pleurodynia in 1949.[4]

Characteristically, in children and occasionally in young adults, there is an acute onset of fever, headache, and anorexia accompanied by severe paroxysmal, knife-like pain in the chest or abdomen which is aggravated by breathing and movement.

During the attack the patient perspires profusely and is extremely prostrated. The temperature rises to 100–102° but may be as high as 104–105°. The disease lasts from four to six days, with typical periods of remissions and exacerbations. The rises and falls in temperature are characteristically sharp, with an intervening period of normal temperature during which the patient feels quite well.[9] The white count is usually at the upper limits of normal, and the differential is not typical.

Although the pain is commonest in the chest and abdomen, pain in the neck, back and extremities may also occur. In the chest the pain is usually low and may be on either side. Almost all patients complain of difficulty in breathing. The pain is made worse on inspiration; therefore respirations are shallow and rapid, rates up to 60 per minute not being uncommon.[12] They are often accompanied by an expiratory grunt and movement of the alae nasi. In some cases pleural rubs have been reported,[7, 12] but the chest is usually normal on examination.

In 30–50% of cases pain predominates in the abdomen,[14] often being localized in the periumbilical region or over McBurney's point. Pain in the left lower quadrant is almost unknown. It is a typical muscle pain which comes on in spasms lasting 5–10 minutes with relief for about half an hour during which the patient appears relatively normal. But during the attack of pain the patient is extremely weak and prostrated, and there is tenderness and rigidity on examination, but no rebound tenderness. Vomiting is rare.[12]

Differential Diagnosis. When the chest symptoms predominate one must consider pneumonia in the diagnosis. Pneumonia may be ruled out by the almost invariable absence of cough, negative chest findings, only a moderate fever with no chills, and the relatively normal white blood count.

When abdominal pain is severe simulation of an acute abdominal condition may be quite striking. The commonest acute abdominal conditions confused with Bornholm disease are acute appendicitis and intussusception.[12] It is quite probable that a large number of the acute appendices seen during the summer months during epidemics of colds and sore throat are really Coxsackie virus infections.[14] If we are to avoid needless surgery in these cases, with its attendant risk, it is obvious that early clinical diagnosis is essential.

Vomiting is quite unusual in Bornholm disease, and if present, it is never persistent.[12] Sneierson was so impressed by the characteristic respiratory difficulty in cases of Bornholm disease he saw that he recommends that in all cases of abdominal pain in children with fever, one should look for the movement of the alae nasi on respiration, and for the presence of an expiratory grunt.[14]

Diagnosis. The difficulty in diagnosis occurs only in isolated cases of Bornholm disease. The typical case should offer little difficulty. The occurrence of muscle pain in children, usually affecting a group, with difficult respiration but normal chest findings, and the characteristic periods of remissions and exacerbations, are so

typical that misdiagnosis should be rare.

Prognosis. In most cases the disease is benign and self-limited. There have been occasional reports of complications such as orchitis, pleurisy, and meningitis.[1]

Treatment. No specific therapy is yet available and the treatment is symptomatic. Antibiotics and chemotherapy are of no value. It has been reported that ACTH and cortisone produce a good response,[2] but it has also been shown that cortisone produces increased susceptibility in adult mice to Coxsackie virus infection.[10]

II. ASEPTIC MENINGITIS

Aseptic meningitis may be caused by a variety of viral agents of which the Coxsackie group B viruses have been shown to be one.

The symptomatology is similar in all cases regardless of the etiological agent. In some cases due to the Coxsackie virus there is complaint of localized muscle pain in the limbs. This is the type of case which is especially important because of its resemblance to poliomyelitis. There have been reports of many cases diagnosed as non-paralytic poliomyelitis on clinical and cerebrospinal fluid findings from which Coxsackie Group B viruses have been isolated from the stool and cerebrospinal fluid.[5, 6, 15] In one case both Coxsackie B and poliomyelitis viruses were isolated from the stool.[1]

The differentiation of Coxsackie B aseptic meningitis from non-paralytic poliomyelitis is impossible clinically.[3]

Like poliomyelitis, Coxsackie virus infection occurs in the summer, and may occur in areas in which poliomyelitis is prevalent. The significance of the association of the Coxsackie B virus and poliomyelitis is not definitely understood, but it appears that the Coxsackie virus cannot cause paralysis by itself.[1]

No specific treatment is available or necessary. The course is uncomplicated and benign, the fever disappearing in 3–10 days.

III. ACUTE MYOCARDITIS

Recently Coxsackie group B viruses have been implicated in acute myocarditis in newborn infants occurring in epidemic fashion (reported by Javett *et al.*[9]). Of the ten infants affected, six died. Clinically the outstanding feature was sudden onset of fever, toxemia, severe tachycardia, with a rapid course ending in death or recovery. The E.C.G. showed depression of T_1. At autopsy on three of the cases the main finding was evidence of patchy myocarditis.

Inoculation of infant mice with brain tissue suspension from two fatal cases produced lesions characteristic of Coxsackie group B infection.

In the same paper reference is made to a similar case with fatal myocarditis occurring in Transvaal.

B. SYNDROMES DUE TO THE COXSACKIE A VIRUSES

I. HERPANGINA

Zahorsky first described this condition as a specific infectious disease in 1920,[17] and gave it this name in 1924.[18] Strains of Coxsackie group A virus were isolated from cases of herpangina in 1951 by Heubner *et al.*[8]

"Herpangina is a specific febrile disease characterized by the appearance of minute papules, vesicles, and ulcers in the throat."[18]

The infection affects children in epidemic fashion only during the summer months. There is an acute onset of fever (102–105°), headaches, anorexia, and vomiting, with pain on swallowing. Minute vesicles appear on the free margin of the soft palate and on the anterior pillar. When these

rupture, 2–6 uleers with punehed out edges surrounded by an inflammatory areola are seen.

Fever eontinues for 3–4 days, and the other symptoms disappear with the fall in temperature. Uleers persist a few days longer.

Uleers may oeeur elsewhere in the bueeal cavity and may at times number as many as 16–20. Mitehell and Dempster[11] reported a ease in which Coxsackie group A virus was isolated from ulcers in the genital area, as well as from the throat (whieh showed the typieal uleeration of herpangina), and from the stool.

Diagnosis. Huebner's eriteria for the elinical diagnosis of herpangina[8] eonsists of fever with a mild uncomplicated course and typical vesieular or uleerated lesions in the faueeal area or the soft palate. The finding of ulcers elsewhere in the oral eavity in the absenee of uleers in these areas does not justify a diagnosis of herpangina.

Thus the diagnosis of herpangina should eause little diffieulty.

Other causes of oral uleeration to be eonsidered are herpetie and aphthous stomatitis and Vineent's angina.

Treatment. Treatment is purely symptomatic, and eomplete reeovery is the rule.

II. THREE-DAY FEVER[16]

This disease is eharaeterized by the sudden onset of fever, headaehe, and malaise, the temperature ranging from 101–104°. The duration of the fever is three days in the majority of the eases. There may be generalized or loealized myalgia. Diarrhea is unusual.

The eourse is benign and the treatment is symptomatie.

III. SUMMER GRIPPE[13]

This is an illness of short duration with myalgia and sore throat.

Summary and Conclusions

1. Well-defined elinieal entities due to the Coxsaekie viruses have been described and the differential diagnosis outlined.
2. In some eases—Bornholm disease and herpangina—possibility of elinieal diagnosis is indieated.
3. The clinical importance of eertain of these diseases has been pointed out.
4. These infections affeet ehildren in partieular, occur in epidemie fashion, are restrieted to the summer and early fall months, and usually have a benign self-limited course.
5. The generally benign nature of these infections appears to be questionable following the report of acute myoearditis assoeiated with Coxsaekie group B infeetions.

Acknowledgment

The author wishes to acknowledge the generous and invaluable assistanee of Dr. A. J. Rhodes and Dr. A. J. Beale.

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ELECTROCARDIOGRAPHY

D. A. SELBY, 5T6

THIS article is intended for students wishing a basic understanding of electrocardiography. It is a survey of well known texts on the subject and dwells on accepted theory. Although electrocardiography is usually considered a subject better left for post-graduate training, there are many beginning practice with little time for such study. One problem of general practice is that physicians are unable to interpret electrocardiograms for their patients. This article is intended to form a foundation for those interested in this problem.

"Electrocardiographic abnormalities are not diseases." The electrocardiogram gives an indication of the electrical activity of the heart. It does not indicate directly the functional ability. An adequately functioning heart may show electrical disturbances, and conversely, an abnormal heart may shown no electrical disturbances. There is a wide variation of normal. Also, there are electrical influences arising outside the heart, and these as well as technical artifacts must be recognized. These variations of the normal cardiogram are more easily realized if the student understands the physiological basis.

THE ELECTROCARDIOGRAPH

Fig. 1 shows the electrocardiograph diagramatically. There are two permanent electromagnets with north and south poles. Straight arrows indicate the lines of force of the magnetic field between the two poles. Arrow "a" indicates the direction of the current through a platinum lined quartz fibre. The curved arrows indicate the lines of force of the electromagnetic field set up about the fibre. The two interacting fields cause a deflection of the fibre toward the observer. The deflection is recorded on a moving film in the camera. The film is marked in graph form and moves at a constant speed. Thus both time and electrical potential can be measured directly. Basically then, the E.C.G. is a sensitive string galvanometer with special photographic equipment and timing device attached.

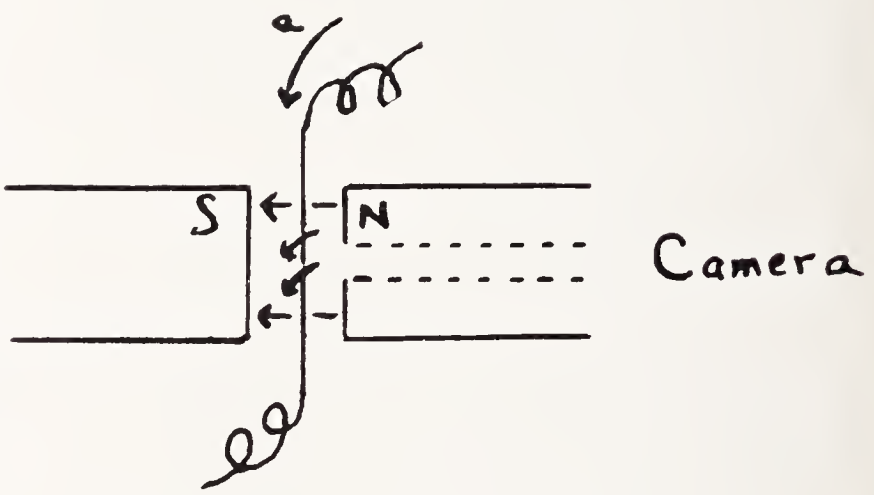

FIG. 1

In the early years of electrocardiography diagnostic information was derived from recognition of various patterns. A knowledge of applied physiology has become more essential to intelligent interpretation of cardiograms. This is particularly true when three types of leads are used routinely. The advent of spatial or three dimensional methods has made the need for an understanding of physiological principles even more necessary. With this in mind some basic principles will be developed.

(a) *Electrical state.* Consider a normal striated muscle fibre. (fig. 2.) The sarcolemmal membrane at rest is a poor electrical conductor. Ions are so arranged that those positively charged (cations) lie on the outside of the membrane while those negatively charged (anions) lie on the inside. The

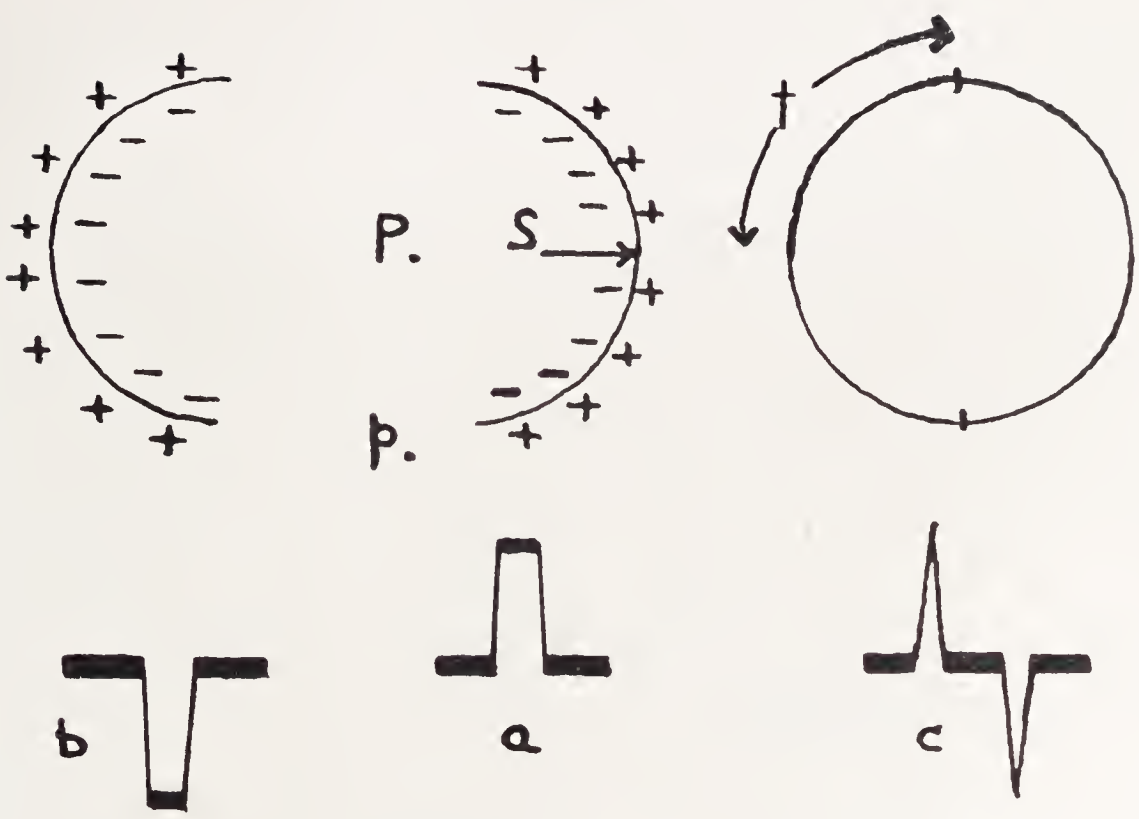

Fig. 2

membrane is said to be *polarized*. For electrical purposes only the charge on the ion is considered. The number of positive charges equals the number of negative charges. A *dipole* consists in a positive and a negative electric charge equal in magnitude and a finite distance apart. In fig. 2a there are many dipoles and each contributes its electrical influence.

An electrical stimulus applied to the point (S) on the surface of the sarcolemmal membrane transforms it to a good conductor and the membrane loses polarity in this activated region. The loss of polarity is due to ion migration across the membrane. Now there is an equal number of positive and negative charges on both sides of the membrane. This change reduces polarity in adjacent resting regions. This reduction of polarity appears to be sufficient stimulus to cause the latter areas to lose the remainder of their polarity (or undergo *depolarization*). Thus the process propagates itself in all directions. *As the wave of depolarization advances, all points in front are relatively positive to all points behind.* Eventually the entire membrane is in the *depolarized state*.

After the fibre has remained in this state for a short time, *repolarization* occurs. This process begins at the point S and spreads as depolarization did previously. When repolarization is complete the fibre is again in the resting state. The electrical changes that constitute the depolarization-repolarization scheme are considered to be by-products of many physical and chemical processes that precede and coincide with fibre contraction. These electrical changes cause the various deflections that are seen in the PQRST sequence.

(b) *Volume conductors.* In fig. 3 a single dipole is placed in a conducting

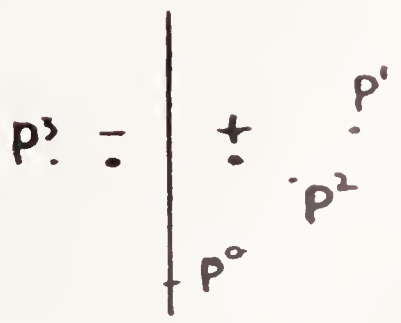

Fig. 3

medium such as normal saline. Any point on a line equidistant between the two charges is at zero or ground potential. Any point to one or other side of this line has either positive or negative potential. As the point is moved further from the charge the potential decreases toward zero or ground potential. It can be shown that potential is inversely proportional to the square of the distance from the charge. In fig. 3 potential at p^0 is zero. If the potential at P^1 is 1 unit then the potential at p^2 is +4 units. Similarly, the potential at P^3 is —4 units. The potential difference between P^2 and P^3 is 8 units. If the two electrodes of an electrocardiograph are placed at points P^2 and P^3 the string is deflected from the centre of the camera slit. The amount of deflection is directly proportional to this potential difference.

In membrane 2a there are many such dipoles and each has its influence over potential. If this hypothetical fibre is placed in a large tank of normal saline, changes in potential may be measured at points removed from the fibre. One electrode of a string galvanometer is placed within the volume conductor and close to the membrane (P—"exploring" electrode). The other electrode is placed sufficiently away from the fibre that the electrical changes of the fibre have little effect over its potential (p—"indifferent" or *reference* electrode). The *law of volume conductors* states that potential at any point is proportional to 1) the angle subtended by all charges on the membrane, and 2) the magnitude and sign of all charges facing the point. In each of figs. 2a and 2b the potential at point P is an equal number of units but of opposite sign. Since in both cases the potential at P is greater than that at p, there is a potential difference between the two points and a current flows through the galvanometer. The resulting string deflections are equal but in opposite directions. If membranes 2a and 2b are now joined to form the complete membrane of 2c, it is evident that the potential at P and p is zero and no current flows.

If membrane 2a is stimulated as before, depolarization and repolarization follows. As depolarization begins, positively charged ions cross the membrane toward P while negatively charged ions move away from P. This means that potential at both P and p is increased positively. By the stated law of volume conductors the rise of potential is greater at P than at p. Potential increases until the depolarization process is complete. This accounts for the sharp upstroke on the attached curve. When repolarization begins the migrations reverse and potential at P and p falls. Again, the fall of potential is greater at P than at p. Potential continues to fall until the membrane returns to the resting polarized state. This accounts for the downstroke of the curve. The complete tracing is known as the monophasic action curve. By reversing the position of the electrodes (fig. 2b) the monophasic action curve becomes the mirror image of that in 2a. If these two curves are superimposed so that they are separated horizontally by the amount of time (t) that it takes the depolarization process to travel from the point S to the second membrane, a diphasic action curve is formed. Alternatively, this curve is produced by stimulating the complete membrane 2c and following the subsequent changes in potential at a point P.

(c) *Application.* The cardiac muscle fibre has no sarcolemmal membrane, but it behaves as if it had an electrical membrane or interface. The basic theory is not altered. Since cardiac muscle is a syncytium, the heart may be considered as two large striated fibres with a special connection. Only changes that occur at the subendocardial and subepicardial surfaces are considered. Changes occurring between these surfaces cancel

one another and have no distant effect. Therefore a lesion that does not involve either surface causes no electrical manifestations. The endocardial surface at rest is relatively negative to the epicardial surface (fig. 2).

The normal stimulus for these changes begins automatically in the S-A node, and spreads through the atrial muscle. It enters the A-V node in the posterior part of the atrial septum and spreads through the specialized conducting tissue in the ventricular septum. The endocardial region of the ventricles is the first area to undergo depolarization. The process spreads from this area at right angles toward the epicardium. As indicated above this wave is preceded by a relatively positive "source" and followed by a relatively negative "sink" (fig. 7). An electrode placed in front of an advancing wave of depolarization is relatively positive to an electrode placed behind the wave.

Repolarization does not begin at the same point where depolarization began as was the case with the hypothetical cell. It actually begins in the subepicardial region near the apex and migrates toward the endocardium. It does not begin at any finite point but rather begins diffusely. Moreover, it takes a longer time to complete itself. For these reasons the ventricular repolarization wave is not a deep inverted spike as in fig. 2c. It is a smooth upright curve with decreased amplitude and longer duration. If, to this modified diphasic action curve, an atrial depolarization wave is added a new curve is formed that resembles the well known PQRST sequence (fig. 4). The atrial repolarization wave (Ta wave) is lost in the ventricular complex.

The heart is situated more to the left side of the body than to the right. The left ventricle is three times as thick as the right ventricle. For these two reasons a point situated on the left shoulder is relatively positive to one situated on the right shoulder during ventricular depolarization. Similar relationships may be worked out for potential changes during depolarization and repolarization at the right and left shoulders and at the symphysis pubis.

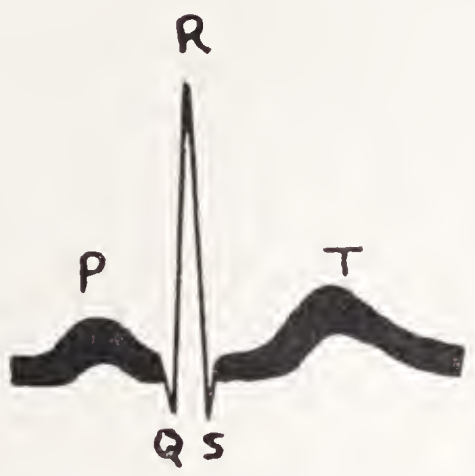

FIG. 4

From this theory the formation of the QRS complex is derived from ventricular depolarization. The formation of the T wave is derived from ventricular repolarization. For practical purposes it appears that the muscle fibre-volume conductor analogy holds true when the heart is considered within the human body.

LEADS

An indirect electrocardiographic lead may be defined as the connection of any two points on the body surface through a galvanometer. There are two kinds of leads in use—bipolar and unipolar.

(a) *Bipolar leads.* These are the classical limb leads I, II, and III. They are called "bipolar" because the record obtained from each lead is the result of changes in potential at two points on the body surface. *An electrode placed on an extremity records change in potential at the point where the limb attaches to the trunk.* Lead I is derived by connecting an electrode on the right arm (RA) to an electrode on the left arm (LA). When the current flows from RA to LA the deflection is positive by convention.

Lead II is derived by connecting RA to an electrode placed on the left leg (LL). When current flows from RA to LL the deflection is positive by convention. Finally, lead III is derived by connecting LA to LL, and when the current flows in this sequence the deflection is also positive. The configuration of the record obtained from the three standard leads is similar to that seen in Fig. 4.

(b) *Unipolar leads.* These are the precordial "V" leads and the unipolar limb leads. They are called "unipolar" because the record obtained is the result of change in potential at one point on the body surface. Until recently this was carried out by placing the exploring electrodes over the cardiac apex and the indifferent or reference electrode on the left leg (lead CF4). It is well known that the potential at this latter point fluctuates throughout the cardiac cycle and is not truly "indifferent." Wilson joined electrodes RA, LA, and LL separately to 5,000 ohms resistances and then united them to form a common electrode. The potential at this electrode shows very little change throughout the cardiac cycle. Today all unipolar leads are taken using Wilson's method. By convention when the exploring electrode is relatively positive to the Wilson electrode, the deflection is positive.

For unipolar chest leads, there are six positions on the chest on which the exploring electrode is placed routinely. They are numbered from one to six. Position 1 is in the fourth interspace to the right of the sternum; position 2 is in the same interspace to the left of the sternum; position 3 is midway between positions 2 and 4; position 4 is in the fifth interspace in the midclavicular line. Positions 5 and 6 are horizontal to position 4 in the anterior and mid-axilliary lines respectively. The exploring electrode and Wilson's electrode are connected through a galvanometer and called leads V_1, V_2 etc. It is evident that the exploring electrode in V_1 position is placed over the right ventricle while that in V_6 position is placed over the left ventricle. During depolarization a positive wave migrates toward the surface. The left ventricle is three times as thick as the right ventricle. For this reason the left ventricle influences a precordial electrode much more than the right.

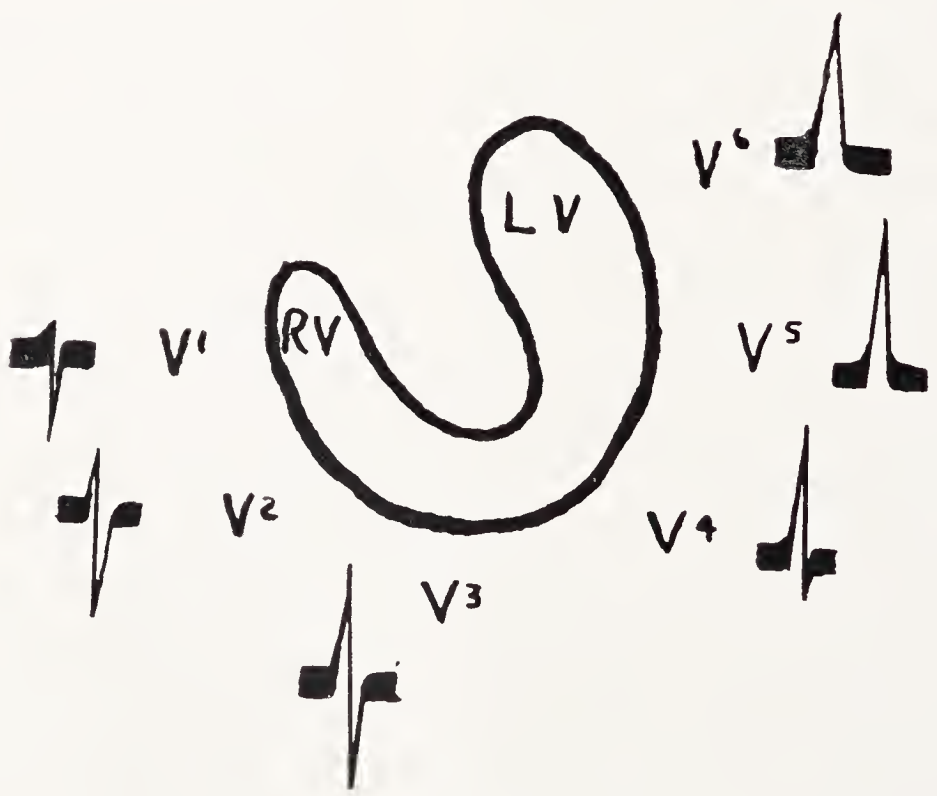

Fig. 5

Hence the main QRS deflection for lead V_1 is negative (down) while that for V_6 is positive (upright). Between V_1 and V_6 there is a gradation of the complexes (fig. 5). The positive and negative deflections for one QRS complex approximately equal one another over the interventricular sulcus. This is seen in lead V_2, V_3 or V_4. Significant variation is suggestive of an underlying pathological process.

Unipolar limb leads. If Wilson's electrode is connected to RA through a galvanometer lead V_R is produced. Similarly, leads V_L and V_F may be derived by connecting LA and LL to the Wilson electrode. The recorded tracing is of low amplitude. It is desirable for clinical purposes to increase the size of the deflections by disconnecting that part of the Wilson electrode to the limb being explored. The leads are then known as the augmented unipolar leads and designated aV_L, aV_R, and aV_F. Although deflection amplitude is increased 50% by this manoeuvre the modified Wilson electrode loses some of its "indifference." There is a close mathematical relationship between the three standard leads and the three unipolar limb leads.

The unipolar limb leads are valuable in judging the electrical position of the heart. This may or may not correlate closely to the anatomical position. Generally there are two extremes of position, the vertical and the horizontal. Most hearts fall in a class somewhere between the two extremes. If the QRS complex of aV_L is tall and positive while that of aV_F is negative, the main mass of muscle must be so situated that the advancing positive depolarization wave effects the left arm electrode much more than the electrode on the left leg. Such is the case in the horizontal heart of late pregnancy. If the QRS complex of aV_F is tall and positive while that of aV_L is negative the main mass of muscle must be so situated that the advancing positive wave of depolarization effects the left leg electrode more than the left arm electrode. This extreme is seen in the tall thin persons with a vertical heart. The main deflection of the QRS complex in aV_R is normally negative because the right shoulder faces the endocardial surface through the A-V valves.

A lead has also been placed in the esophagus and within the heart itself during cardiac catheterization. These leads are used for experimental work and are required only rarely for clinical purposes. It should be stressed that the term "exploring" electrode can be taken literally. Electrodes have been placed over many points of the body surface and some of these extra positions have been useful clinically.

ELECTRICAL AXIS

At any instant during the cardiac cycle, innumerable dipoles are contributing their effects to the electrical field about the heart. Each charge of the dipole, the positive and negative, may be considered to exert a force which is proportional to the magnitude of each charge. The dipole exerts its greatest force along a line that connects the two charges. The direction of the force is from the negative to the positive charge. This force may be represented graphically by a *vector* that has both magnitude and direction. The *manifest vector* is the resultant sum of all dipolar vectors at any one instant during the cardiac cycle. As pointed out above, the number and position of all cardiac dipoles is constantly changing during the P-T interval. It follows that the manifest vector must also change both in direction and magnitude during the interval (fig. 7). For clinical purposes it is useful to calculate the mean electrical axis for ventricular depolarization. The mean electrical axis for ventricular depolarization is the *mean manifest vector* for the QRS complex. This may be calculated by using the three standard (bipolar) limb leads.

The right and left shoulders and the symphysis pubis are considered to lie in the coronal plane. When these three points are connected they form an equilateral triangle (Einthoven's triangle). In fig. 6a the points of electrode contact (RA, LA, LL) and the midpoints of

the three lead sides are indicated on an equilateral triangle. The heights of the QRS complexes of the three bipolar leads are measured. Using a convenient ratio they are laid on the proper lead line to one or other side of the midpoint. The direction from the midpoint depends upon the relation of the QRS complex to the base line (see LEADS). Perpendiculars are dropped from all six points and intersected at two new points. The resulting veetor is a manifest vector of ventricular depolarization. It has direction, magnitude and sign.

To calculate the mean manifest veetor or mean electrical axis a similar process is used. Instead of employing the heights of the three QRS complexes, the areas under the complexes are used (fig. 6a).

A modification of Einthoven's reference system is preferable. It is called the triaxial reference system and is formed by superimposing the three midpoints of each side of the equilateral triangle (fig. 6b). Each of the three axes corresponds to one lead. The central point of intersection divides eaeh line into positive and negative sides. Angles are measured with reference to the positive segment of thc horizontal axis (lead I). Any angle above the horizontal axis has a negative value, while any angle below the horizontal axis has a positive value. All measurements are made from the central point. Regardless of which reference system is used, the manifest vectors and the mean electrical axes have the same lengths and directions.

It is useful to measure the angle (α) between the mean electrical axis and the lead I axis. Thc average normal adult angle measures 58°. The upper limits of normal variation are usually considered as −20° to +100°. If the angle that the electrical axis forms with the lead I axis is less than −20° or more than +100°, thc electrical axis is said to show deviation to the left or right respectively. This deviation may or may not correlate closely to anatomical axis shift. Right axis deviation is seen normally in infants. It is seen in diseased states that cause the right ventricle to hypertrophy and/or dilate e.g. mitral stenosis, pulmonary stenosis. Right axis deviation is also seen in right bundle branch block. Left axis deviation is seen normally in persons with horizontal hearts e.g. the heart of late pregnancy. It is seen in pathological states that cause the left ventricle to hypertrophy and/or dilate and in left bundle branch block.

In the same fashion the mean electrical axis for the T wave is also calculated. Using these two electrical axes for adjacent sides, a parallelogram is constructed. By joining the central point of the reference system to the opposite corner of the parallelogram, a vector known as the *ventricular gradient* is formed. In the hypothetical system of fig. 2c it is evident that the electrical axes for depolarization and repolarization are equal and placed at 180° to each other. In this system both processes began at the same point and travelled at the same rate. There is no ventricular gradient. The fact that in reality there is a gradient proves that the two processes do not begin at the same point and travel at the same rate. The ventricular gradient points along the line where there is greatest lack of uniformity of the depolarized state. The ventricular gradient is normally within 20° of the base-apex axis.

The three electrodes of the classical bipolar leads lie in the frontal (coronal) plane. Hence all vector caculations lie in the frontal planc. Since these vectors seldom lie in this plane, the final calculations are the frontal projections of the true vectors. This is demonstrated in sagittal section in fig. 6c. Vector 1 is the true

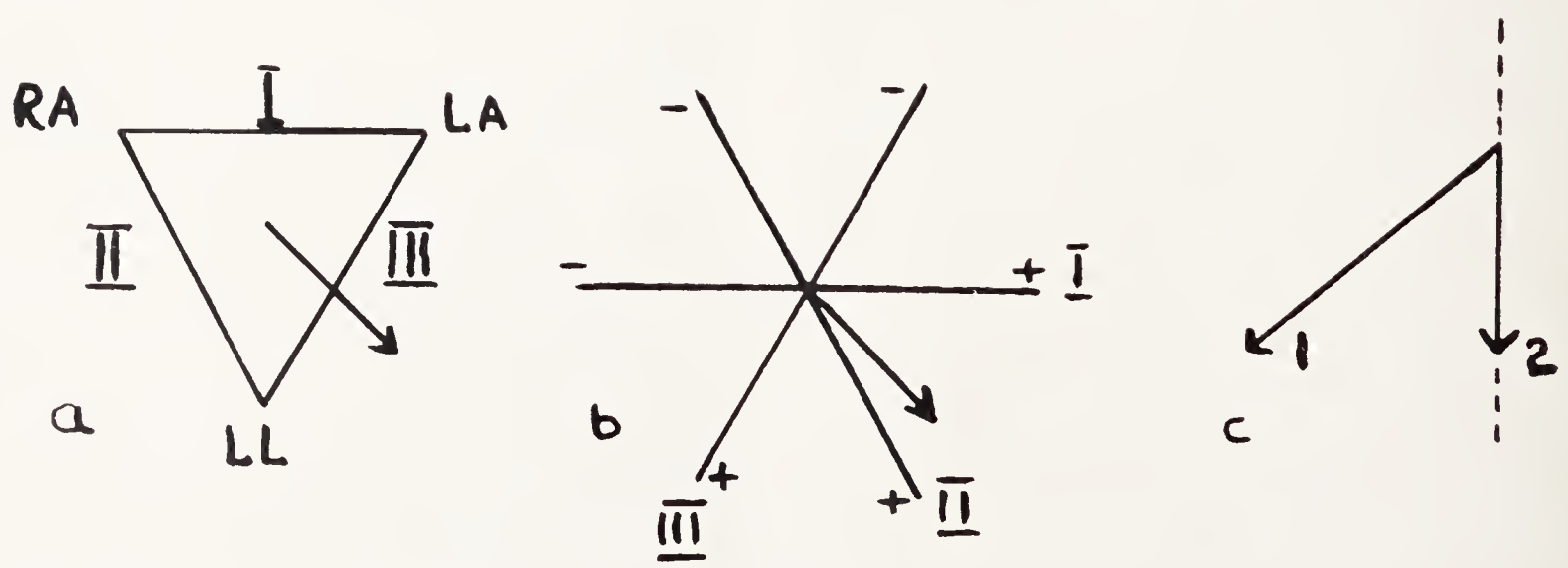

Fig. 6

vector and vector 2 is the frontal projection. The true vector is considerably longer than its projection.

VECTORCARDIOGRAM

If all the tips of manifest vectors for ventricular depolarization are connected, a closed loop is formed. The loop is closed because the QRS complexes both start and end at the isoelectric (or base) line. This loop is known as the QRS loop or the vectoreardiogram. Closed loops may also be drawn for the P, T, and U waves. The subject whereby all these loops are considered is known as spatial vectoreardiography. Although normal and pathological loops have a somewhat typical appearance it is difficult as yet to evaluate the subject for clinical purposes.

This paper so far has attempted to illustrate some important theoretical aspects with which the student should be familiar. The study is incomplete but is sufficiently advanced to permit mention of some clinical entities.

MYOCARDIAL INFARCTION

One of the chief values of the cardiogram is to determine the presence and location of an infarct. The principles involved in this and some other conditions are described briefly.

Infarcts may occur in any position in the atrial or ventricular myocardium. They may be single or multiple. Electrical changes depend upon (1) position, (2) size, (3) speed of onset and healing, (4) age, and (5) complications. Position may be classified into (a) position of infarct relative to heart surface and (b) position of infarct relative to endocardium and epicardium. Anterior infarcts differ from posterior infarcts. Infarcts that are close to the endocardium differ from those that are close to the epicardium and from those that transect the whole thickness of the ventricular musculature (transmural). As has been suggested above infarcts that involve neither surface (intramural) show no electrical effects. Age, size and onset are considered below. Complications such as pericarditis, bundle branch block or arrhythmia obscure changes due to the infarct alone.

It is important to understand the changes that occur when a region of myocardium loses its blood supply suddenly. Immediately following arterial occlusion the involved region becomes *ischemic*. After a variable period, a smaller area within the latter becomes further devitalized or *injured*. Finally the central portion becomes *necrotic*. This process is variable and there are no finite lines separating the three zones. While the central area is undergoing necrosis, the ischemic area may be enlarging or returning to normal. The whole involved area is surrounded by normal myocardium except where endocardium or epicardium limit the extent of the infarct. The whole involved part exists in *three dimensions*.

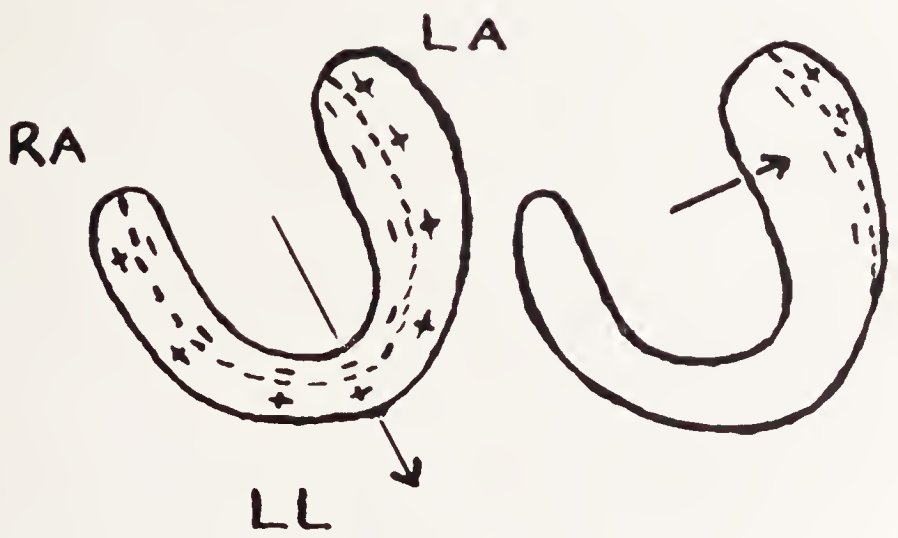

FIG. 7

(a) *Anterior Infarction.* For an example, suppose that the anterolateral region of the left ventricle becomes infarcted subepicardially. When this area becomes ischemic, the affected myocardium remains in the depolarized state for a longer period than it would if it were normal. Also, repolarization is slower. Repolarization begins normally in the apical subepicardial area. With ischemia of this region it begins in the subendocardial region. Since ventricular depolarization remains unchanged, only T wave changes are seen when the exploring electrode of a unipolar chest lead is placed directly over the ischemic region, the T wave of the record becoming inverted. This occurs because the repolarization process is now spreading toward, rather than away from, the overlying electrode. This effects an area of relative negativity at the overlying electrode so causing inversion of the T wave.

When a part of the ischemic area becomes injured the latter region is in a partially depolarized state even though it is at rest. This causes the potential at the exploring electrode to become relatively negative to that at the indifferent or reference electrode. Because of the potential difference, a current passes through the galvanometer. This current is known as the "current of injury." When the surrounding normal muscle undergoes depolarization, the injured muscle passes from its partially depolarized state to complete depolarization. Hence the interval between the QRS and T waves (S-T segment) is isoelectric as usual. Before a clinical electrocardiogram is taken, all steady currents that tend to displace the galvanometer string away from the centre of the camera slit are neutralized. The current of injury is also neutralized. Hence while the exploring electrode is isoelectric to the indifferent electrode between the end of depolarization and the beginning of repolarization, the current that neutralized the current of injury is now unopposed and causes a deflection of the galvanometer string upward. The S-T segment is displaced upwards even though there is no real potential difference between the exploring and indifferent electrodes.

Necrotic muscle remains in the depolarized state at all times. It undergoes no changes during the cardiac cycle. The effect upon potential at the overlying electrode depends upon the amount of necrotic and normal muscle in the left ventricle. If the amount of necrotic tissue is large, the left ventricle has relatively little influence over potential at the overlying electrode. Conversely, if the amount of necrotic tissue is small, the left ventricle maintains its influence over potential. In wide transmural infarction, the normal QRS complex is replaced by one entirely negative wave known as a QS wave. This occurs because only the right ventricle is influencing the exploring electrode and its depolarization wave is moving away from the exploring electrode. If there is some normal muscle underlying the infarct, the QRS complex consists of a positive R wave which is roughly proportional to the amount of remaining normal muscle. The depth of the negative S wave is roughly inversely proportional to the amount of remaining normal muscle. Unless the infarct is intramural the amplitude of the R wave is always reduced.

These changes occur when the exploring electrode is placed directly over the infarct. As the electrode is moved away the changes become less pronounced. It follows that in a suspected case of myocardial infarction the exploring electrode may have to be moved from one place to another before the typical results are found. Indeed in some cases they are never found.

From the above reasoning the changes in the bipolar limb leads may be predicted. During depolarization, RA is more positive, and LA less positive than

usual. The amplitude of the R wave in lead I is reduced. If RA becomes relatively positive to LA, as in severe infarction, there is an initial negative wave in the QRS complex of lead I. This is known as a Q_1 wave. For the same reasons as above, the S-T segment is displaced upwards. The T wave becomes flattened, isoelectric or inverted. This occurs because repolarization is now moving toward LA rendering it relatively negative to RA. If changes in potential are compared for electrodes LA and LL, the lead III changes become evident. The QRS complex has a low R wave and a deep S wave. There is depression of the S-T segment and flattening of the T wave. These bipolar limb lead changes for anterior infarction constitute the Q_1 T_1 pattern. Since the unipolar limb leads are so closely related to the bipolar limb leads, their changes present no problem.

To this point, only changes seen in the acute stage have been mentioned. If the infarct develops gradually these dramatic signs do not appear. Instead, the changes seem to depend upon the stage to which the pathological lesion has developed. There may be signs of ischemia, injury and necrosis alone or in combination. When either healing or extension begin these changes alter. After a period varying from hours to days the uncomplicated infarct begins to show electrocardiographic signs of healing. The injured muscle either progresses to necrosis or reverts toward normal. Since there is no current of injury there is no S-T segment shift. This is the earliest change seen. It often happens that the first electrocardiogram is taken at this time, and the possibility of infarction without S-T shift should be kept in mind. In the chronic stage, only the QRS and T wave abnormalities remain. Over a long period the T wave signs may or may not return to normal. The QRS changes generally persist. On occasion all evidence of the lesion disappears leaving a normal cardiogram. These changes should always be followed.

In the above example the infarct was arbitrarily placed in the subepicardial region. If the infarct is placed in the subendocardial region, the electrocardiographic signs are changed. Ischemic, injured, and necrotic muscle retain the same properties. When the exploring lead of a unipolar chest lead is placed over a subendocardial ischemic region, the T wave remains upright. This occurs because repolarization begins subepicardially and proceeds in the normal direction. When this region of muscle becomes injured, the current of injury causes depression of the S-T segment. This occurs because at rest the exploring electrode is relatively negative to the Wilson electrode. The current of neutralization (see above) is unopposed during the interval between the end of depolarization and the beginning of repolarization. This current is responsible for depression of the S-T segment. With necrosis of muscle the initial QRS deflection is negative because the right ventricle predominates during the early part of depolarization. The later part of the QRS complex is positive if there is normal muscle overlying the infarct. Changes in the limb leads may be reasoned in a similar manner.

(b) *Posterior Infarction.* The involved muscle undergoes the same pathological process in posterior infarction as in anterior infarction. The reasoning for the various changes will not be reiterated. Instead of a Q_1T_1 pattern, there is a Q_3T_3 pattern in the bipolar leads. The precordial leads are of less practical value in the diagnosis of posterior infarction than anterior infarction. A routine precordial electrode cannot be placed directly over the infarct. The R wave may not be abnormal. In some cases the S-T segment is displaced and the T wave is tall.

Occasionally there may be more than

one infarct. The effect of the most recent and of the largest injury tends to predominate the completed electrocardiogram.

It has been shown that to each of the three degrees of pathological involvement certain electrocardiographic changes are assigned. Since an infarct does not exist unless there is muscle necrosis, an electrocardiographic diagnosis of myocardial infarction cannot be made unless there are QRS changes present. This point is most important when evaluating infarcts which are not accompanied by pain. The value of this reservation is evident when differentiating a severe anginal attack from an infarct. Other diagnostic problems include pericarditis and pulmonary embolism. If the patient is receiving digitalis, dependence on QRS changes is again necessary.

ANGINA PECTORIS

The symptoms of this condition are considered to be due to arterial insufficiency in the subendocardial region. Since the insufficiency is temporary there is no tissue necrosis and therefore no changes in the QRS complex that suggest infarction. There may be QRS changes that indicate the cause of the angina (e.g. left axis deviation in hypertension). The anginal attack is accompanied by abnormalities that suggest ischemia and injury. These are (1) depression of all S-T segments and (2) alteration of T waves in all leads. With release of the insufficiency those changes may disappear.

ACUTE PERICARDITIS

The electrocardiographic changes are due to diffuse subepicardial injury. There are no alterations in the QRS complex that suggest infarction. Elevation of the S-T segments and flattening or inversion of the T waves are seen typically in leads I, II and V_4.

ACUTE PULMONARY EMBOLISM

If the embolus is large, a cardiogram taken in the acute stage may show abnormalities that are almost identical to those of posterior infarction. The electrocardiographic changes of pulmonary embolism are usually transient while those of infarction are usually permanent. Consecutive records differentiate the two conditions. This example serves to emphasize the principle that the investigation of myocardial infarction requires continuous re-evaluation during the critical period.

DIGITALIZATION

Electrocardiographic changes vary to some extent with the intensity of digitalization. The earliest change is prolongation of the P-R interval, with spooned negative T waves. Generally the S-T segment is displaced in an opposite direction to the main QRS deflection. Bipolar T wave changes occur with more intense digitalization. Toxic signs include premature beats, variable degrees of A-V block and ventricular arrhythmias. There are no changes that suggest necrosis of muscle.

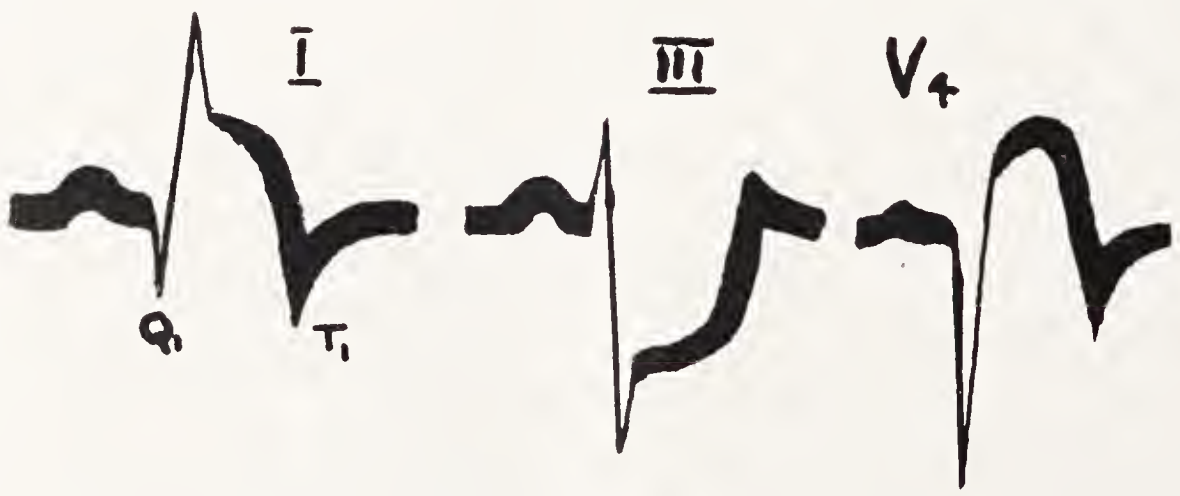

FIG. 8

SUMMARY

It is stressed that this article is not presented for its diagnostic use. If the student understands the basic theory he is in a position to correlate clinical findings with electrocardiographic abnormalities. Electrocardiography is most useful when correlated with history and physical examination. Whenever a cardiogram is ordered there should be some definite indication. They are not ordered routinely.

The substance of the article has included:

(1) Explanation of the electrocardiograph.
(2) Development of the depolarization-repolarization theory.
(3) The three types of leads used at the Toronto General Hospital at this time.
(4) Discussion of electrical axis and its application.
(5) Reference to spatial vectorcardiography.
(6) Some clinical applications of the presented theory.

ACKNOWLEDGMENT

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ABSTRACTS

Rounded Intrathoracic Lesions: Springer, D. W., Geiger, P. E., and Langston, H. T., Amer. J. of Roentgenology **74**: 827, 1955.

This paper presents twenty illustrative cases of a group of patients studied in 1952–53 having a wide variety of intrathoracic lesions which exhibited a common discrete, circumscribed, solid-appearing, smooth-edged density on chest roentgenograms. A short history of each case is given with accompanying roentgenogram photographs and photomicrographs of the respective pathology.

In spite of exhaustive pre-operative procedures including roentgenograms, it was not possible to conclude the exact nature of these conditions prior to surgical removal and pathological examination. The pathologically proved diagnoses of these lesions were:

Encapsulated empyema—1
Benign fibrous epithelioma—1
Thymic cyst—1
Teratoma, anterior mediastinum—1
Pericardial cyst—1
Adenocarcinoma, primary undetermined—2
Metastatic carcinoma—2
Metastatic sarcoma—1
Primary carcinoma—6
Primary sarcoma—2
Granuloma, probably tuberculous—3

It is concluded that rounded intrathoracic lesions having similar roentgenograms can be correctly appraised only with the aid of biopsy obtained at thoracotomy.

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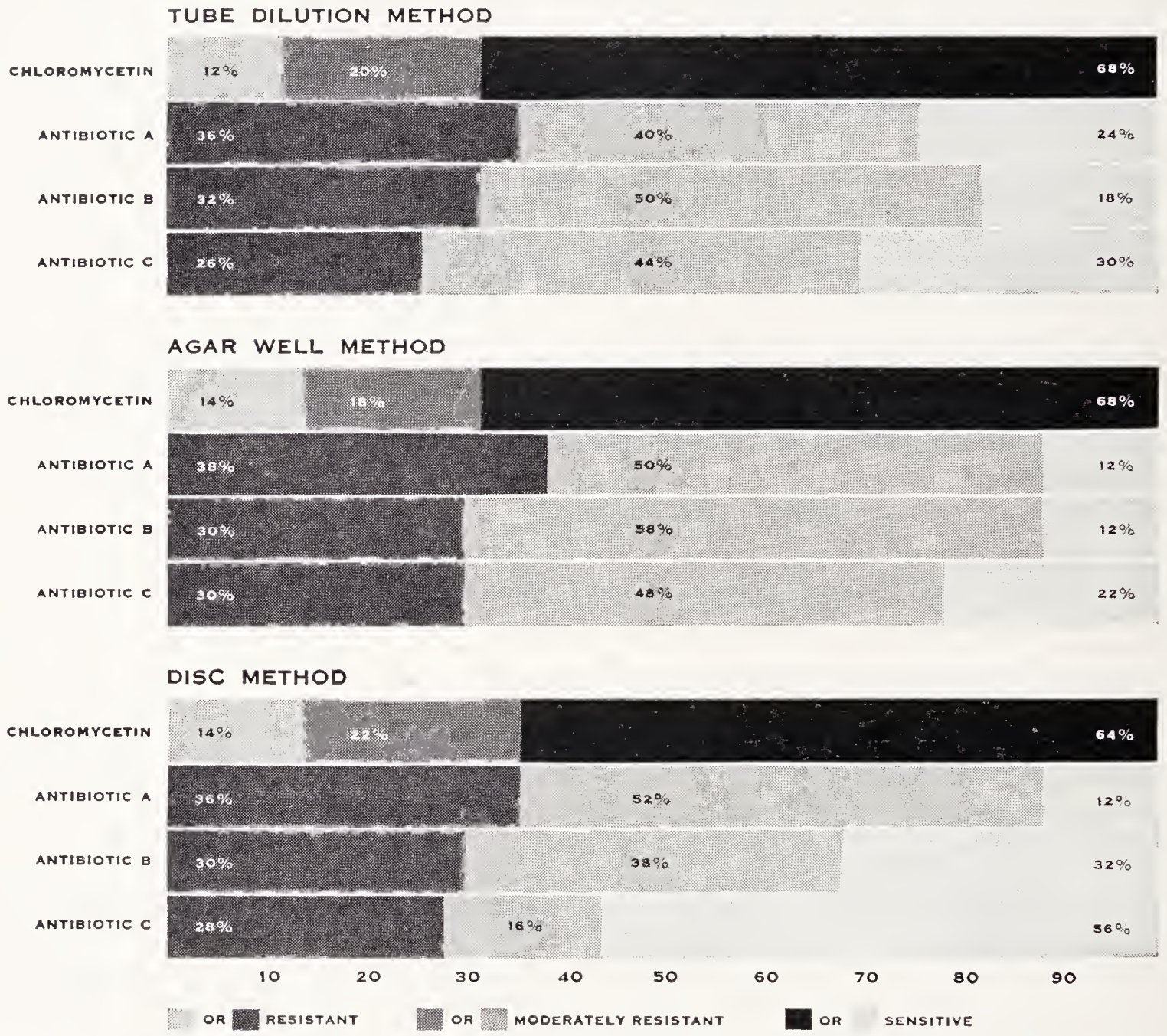
SENSITIVITY OF 50 GRAM-NEGATIVE BACILLI* TO CHLOROMYCETIN AND THREE OTHER MAJOR ANTIBIOTICS TESTED BY THREE METHODS



*Breakdown of gram-negative bacilli—Coli: 11; Proteus: 10; *Klebsiella pneumoniae:* 9; Aerobacter: 7; Pseudomonas: 7; Achromobacter: 2; Paracolon: 2; *Salmonella typhosa:* 1; *Bacterium anitratum:* 1. Adapted from Branch, A.; Starkey, D. H.; Rodgers, K. C., & Power, E. E.: Antibiotics Annual, 1954-1955, New York, Medical Encyclopedia, Inc., 1955, p. 1125.

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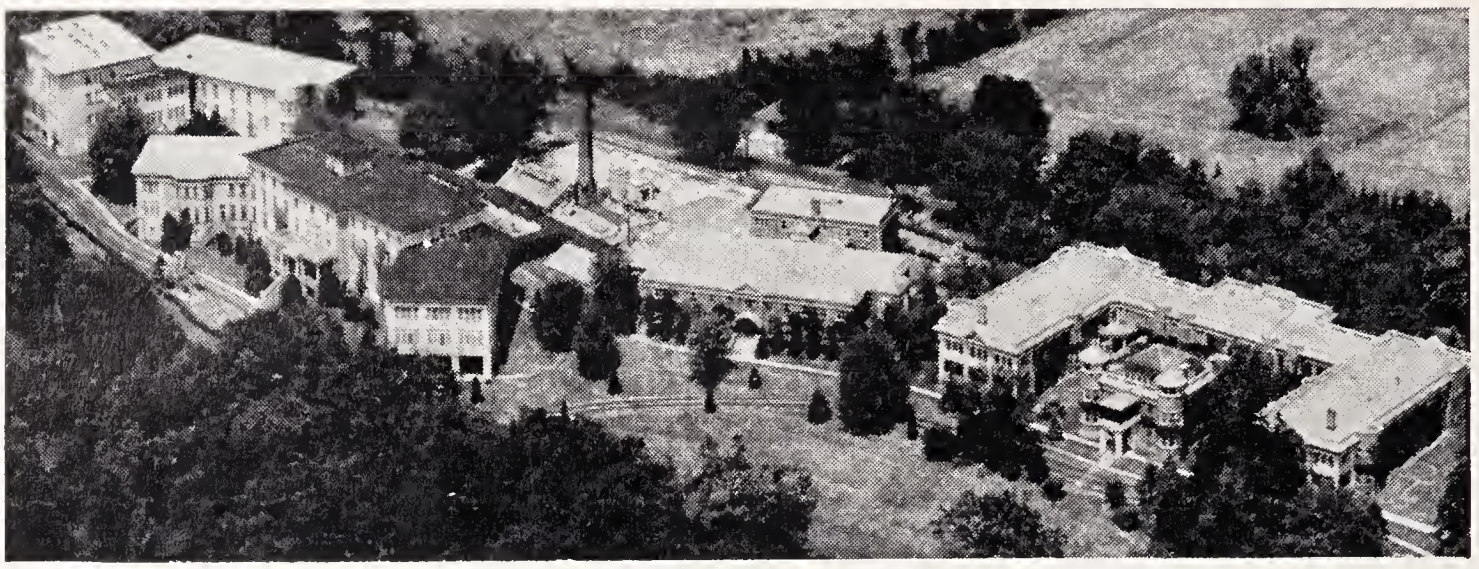

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